To: Cook, Dr. Mary[/O=PURDUE/OU=PURDUE US/CN=Sales and Marketing - Field/cn=CookM]; Fujimoto, Dr. Darlene[/O=PURDUE/OU=PURDUE US/CN=Sales and Marketing - Field/cn=FujimotD]; Plant, Dr. Ruth[/O=PURDUE/OU=PURDUE US/CN=RECIPIENTS/CN=PlantR]; Barreuther, Alan[/O=PURDUE/OU=PURDUE US/CN=Sales and Marketing - Field/cn=BarreutA]; Chudzik, Dr. Gregory[/O=PURDUE/OU=PURDUE US/CN=Sales and Marketing - Field/cn=ChudzikG]; Dube, Dr. James[/O=PURDUE/OU=PURDUE US/CN=RECIPIENTS/CN=DubeJ]; Gainey, Dr. Matthew[/O=PURDUE/OU=PURDUE US/CN=SALES AND MARKETING - FIELD/CN=GAINEYM]; Geiwitz, Dr. Allen[/O=PURDUE/OU=PURDUE US/CN=Sales and Marketing - Field/cn=GeiwitzA]; Griffin, Dr. Cherylnn[/O=PURDUE/OU=PURDUE US/CN=RECIPIENTS/CN=GriffinC]; Keane, Teresa[/O=PURDUE/OU=PURDUE US/CN=Sales and Marketing - Field/cn=KeaneT]; Kowalski, Dr Maribeth[/O=PURDUE/OU=PURDUE US/CN=Sales and Marketing - Field/cn=KowalskM]; Ladd, Lori[/O=PURDUE/OU=PURDUE US/CN=Sales and Marketing - Field/cn=LaddL]; LaPerriere, Dr. Jacqueline[/O=PURDUE/OU=PURDUE US/CN=Sales and Marketing - Field/cn=LaPerriJ]; Miller, Lisa Dr.[/O=PURDUE/OU=PURDUE US/CN=Sales and Marketing - Field/cn=MillerLi]; Raebel, Dr. Shelley[/O=PURDUE/OU=PURDUE US/CN=RECIPIENTS/CN=RaebelS]; Wagley, Dr. William[/O=PURDUE/OU=PURDUE US/CN=Sales and Marketing - Field/cn=WagleyW]
Cc: DaBronzo, Dr. Joseph[/O=PURDUE/OU=PURDUE US/CN=RECIPIENTS/CN=DaBronzJ]; Schiff, Deborah[/O=PURDUE/OU=PURDUE US/CN=RECIPIENTS/CN=SchiffD]
From: Dover, Dr. Kristi
Sent: Mon 7/1/2002 5:00:40 PM
Subject: Should I Dispense Programs
Should I Dispense.zip
Should I Dispense one hr.zip

Dear Colleagues,

Hope this message finds you well.

Attached please find the current zip files for the one-hour and two-hour "Should I Dispense" programs. Please note, some slides may be currently "hidden".

Have a fantastic Fourth.

Kristi

PLAINTIFF TRIAL EXHIBIT
P-27213_00001

Produced Natively

What concerns do you have?

Legit script

Legit doctor

Legit patient

Drug choice

Drug dose

Evokes a lot of emotion:

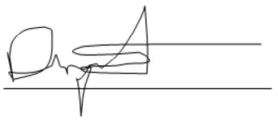
friend / family with: chemical dependency

pain

Dr. Hxrrrq Dcvsztl, M.D.
1000 Main Street
Nowhere, USA 10000
(999) 555-1212

1 pound

Morfeen



The tenets of legal prescribing

- A legal prescription for a controlled substance must be:
  - issued for a legitimate medical purpose
  - by an individual practitioner acting in the usual course of their professional practice
  - documented in the medical records

Example 1

- Prescribing benzodiazepines via telephone to a patient you've never met

Example 1

- Prescribing benzodiazepines via telephone to a patient you've never met
  - medical experts would testify that no physician-patient relationship existed
  - therefore, this was not legitimate medical purpose

Example 2

- A nurse stops a physician in the hospital and asks for a small amount of a prescription drug and the physician writes the prescription without a proper H&P and documentation

Example 2

- A nurse stops a physician in the hospital and asks for a small amount of a prescription drug and the physician writes the prescription without a proper H&P and documentation
  - medical experts would testify that no physician-patient relationship existed
  - therefore, this was not legitimate medical purpose

Example 3

- A dentist prescribes an opioid to an adult patient (friend) for low back pain following appropriate history and physical exam

Example 3

- A dentist prescribes an opioid to an adult patient (friend) for low back pain following appropriate history and physical exam
  - medical experts would testify that even though this was a legitimate medical purpose, it was outside the usual course of professional practice

Drug Scams

- Practitioner prescribes for deceased patients and then picks up medication for personal abuse
- Abuser posing as a pharmacist or regulator calls receptionist to obtain DEA numbers of all the prescribers in the practice
- Scams are only limited by the imagination of the drug seeker

Example of patient filling too early or at multiple pharmacies.

DIFFERENTIAL DIAGNOSIS:

Abuse

Chemical Dependence

Poor pain control

Pseudoaddiction

- Pseudoaddiction: Appropriate drug-seeking behavior for the purpose of pain relief, not for abuse.
  - Quickly differentiated from true abuse when an appropriate increase in dose stops the behavior.
- The potential for opioid abuse, while small, exists nonetheless, and all clinicians must be aware of the warning signs.

Pseudoaddiction

- Addicts normally exhibit profound "drug-seeking" behavior.
- "Drug-seeking" behavior does not always indicate abuse.
- It may indicate that a patient is an appropriate opioid candidate but is not receiving a dose sufficient to maintain lifestyle and functional level.
- Oncology setting: "Drug-seeking" behavior to obtain effective pain relief has been referred to as a "pseudoaddiction."[23]
- The phenomenon of "pseudoaddiction" has been recognized by The American Society of Addiction Medicine.[24]

23. Weissman DE, Haddox JD. *Pain.* 1989;36:363-366.
24. American Society of Addiction Medicine. *Public Policy Statement on Definitions Related to the Use of Opioids in Pain Treatment.1997.*

Physical Dependence

"Physical dependence on a controlled substance is a physiologic state of neuro-adaptation which is characterized by the emergence of a withdrawal syndrome if drug use is stopped or decreased abruptly, or if an antagonist is administered."

Physical dependence is an expected result of opioid use and, by itself, does not equate with addiction.

(Federation of State Medical Boards of the United States, Inc. *Model Guidelines for the Use of Controlled Substances for the Treatment of Pain.* Euless, TX; 1998)

Addiction

Addiction is a primary, chronic, neurobiologic disease, with genetic, psychosocial, and environmental factors influencing its development and manifestations.

It is characterized by behaviors that include one or more of the following:

impaired control over drug use, compulsive use, continued use despite harm, and craving

Approved by the Boards of Directors of the AAPM, APS, and ASAM, February 2001

Drug Seeking Behavior

- Wants appointment toward end of office hours or telephones/arrives after regular business hours
- Insists on being seen immediately or demands immediate action. Says they are in a hurry to catch a plane, or late for a business meeting

Drug Seeking Behavior

- Not interested in having physical examination or undergoing diagnostic tests
- Unwilling to give permission to obtain past medical records
- Unable to recall hospital or clinic where past records are kept, or states they are out of business or burned down
- Unwilling or unable to give names of past health care professionals

Drug Seeking Behavior

- Claims to be from out of town and to have lost prescription, forgotten to pack medication or says that it was stolen
- Exaggerates or feigns medical problems
  - Complains of renal colic (pricks finger to add blood to urine specimen)
  - Complains of migraine, tic or toothache
- Recites textbook symptoms or gives very vague medical history

Besides hurting themselves…The behavior of chemically dependent individuals often directly impacts the appropriate medical care that is available for legitimate pain patients.

Pain is a major, yet largely avoidable, public health problem.[1] In most patients with chronic painful conditions (eg, cancer, arthritis, back disorders, headache), usually it is the pain, not the underlying pathology, that limits their ability to function and lead a productive life.[2]

[1]Joint Commission Focuses on Pain Management [press release]. Oakbrook Terrace, Ill: Aug 3, 1999.

[2]Bonica JJ. General considerations of chronic pain. In: *The Management of Pain*. 2nd ed. Philadelphia: Lea & Febiger; 1990:180-195.

Slide References

Greenwald BD, Narcessian EJ. Opioids for managing patients with chronic pain: community pharmacists' perspectives and concerns. *J Pain Symptom Manage* 1999;17:369-375.

Bonica JJ. General considerations of chronic pain. In: *The Management of Pain*. 2nd ed. Philadelphia: Lea & Febiger; 1990:180-195.

Possible Adverse Effects of Undertreated Pain

Physiological

Increased catabolic demands lead to

- Muscle breakdown
- Poor healing
- Weakness

Impaired respiratory effort increases

- Risk of atelectasis

Impaired limb movement increases

- Risk of thromboembolic events

Other potential physiological consequences

- Water retention
- Inhibited GI motility
- Hypertension, tachycardia, tachypnea (acute)

Adapted from AHCPR Guidelines, 1992,[11] 1994[12]

Possible Adverse Effects of Undertreated Pain

Psychological

Negative emotions including

- Anxiety
- Depression

Other psychological effects

- Sleep deprivation
- Existential suffering

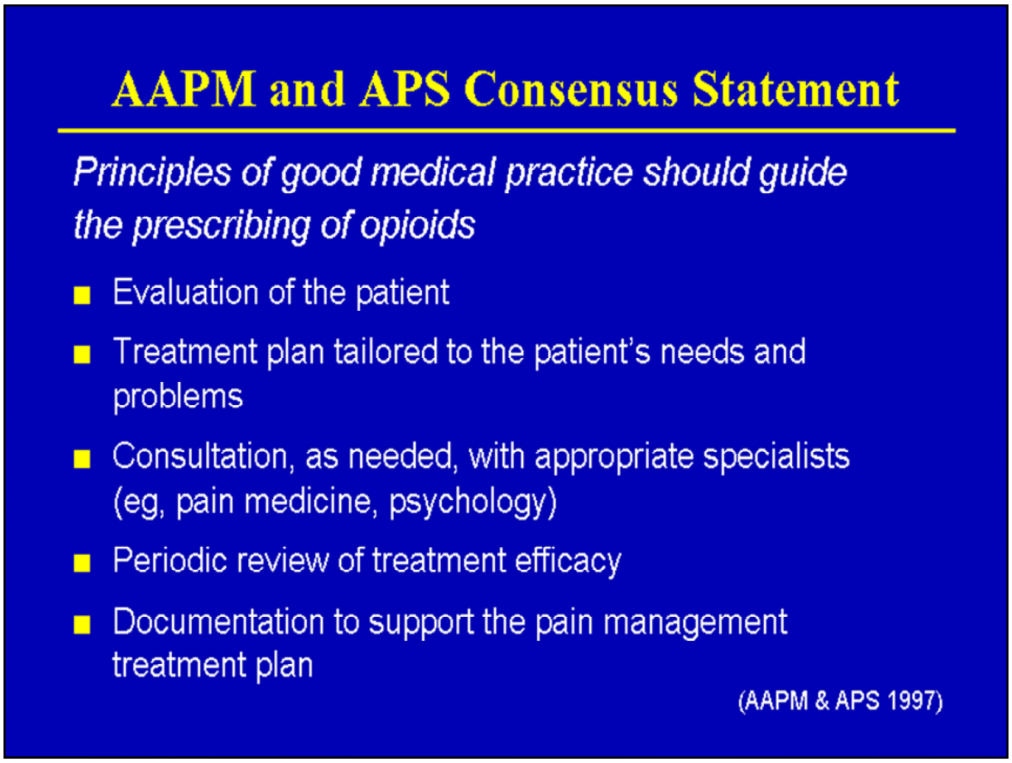
Immunological

Impaired immune response

- Decreased natural killer (NK) cells

Adapted from AHCPR Guidelines, 1992,[11] 1994[12]

Paradigm Shift in
Pain Management



Chronic pain is often inadequately treated

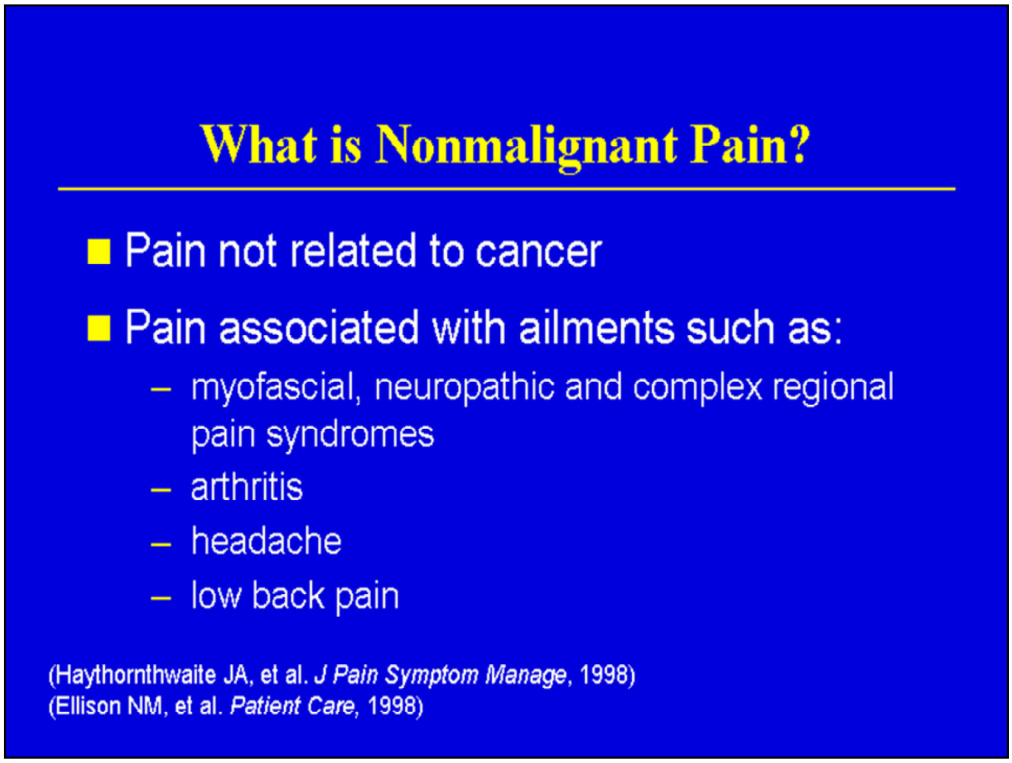
Using opioids for chronic pain is legitimate medical practice

Concerns regarding addiction, tolerance, and respiratory depression lead to underutilization

Accepted principles for opioid use should be promulgated

Principles of good medical practice should guide prescribing

Adverse events can usually be managed, or diminish with use



Over 30 million Americans suffer from chronic pain of a nonmalignant origin.[8]

[8]Holmquist GL. The appropriate use of opioids in the management of chronic pain: a pharmacist's perspective. *Pharmacy Times* 1999;29:3-11.

Slide References

Haythornthwaite JA, Menefee LA, Quatrano-Piacentini AL, Pappagallo M. Outcome of chronic opioid therapy for non-cancer pain. *J Pain Symptom Manage* 1998;15:185-194.

Ellison NM, Lipman AG, Patt RB, Portenoy RK. Opioid analgesia: an essential tool in chronic pain. *Patient Care* 1998;32:2-11.

Interdisciplinary Team Members

Physicians

Preferably board certified by American Board of Pain Medicine or of Anesthesiologists; have earned the American Board of Anesthesiology qualification in pain

- Medical management
- Most common professionals:
  - Anesthesiologists
  - Neurologists
  - Physiatrists
  - Psychiatrists

Interdisciplinary Team Members

Mental health professionals

- Cognitive behavioral therapy
  - Addresses learned pain behaviors
- Management of psychological disorders and somatization
- Most common professionals
  - Psychologists with advanced training in behavioral medicine
  - Sometimes social workers

Interdisciplinary Team Members

Nurses

- Patient education
- Case management

Rehabilitation specialists

- Physical therapy
- Occupational therapy
- Recreational therapy
- Vocational counseling

Interdisciplinary Team Members

Pharmacists

- Obtain detailed medication histories
- Monitor and manage drug therapy (pharmaceutical care plan)
- Manage cessation of ineffective medications
- Provide patient education
- Provide drug information/education to team members

These multidisciplinary teams care for some of the most complicated patients.

They have rules, contracts, urine tox screens, etc. You can set your own rules.

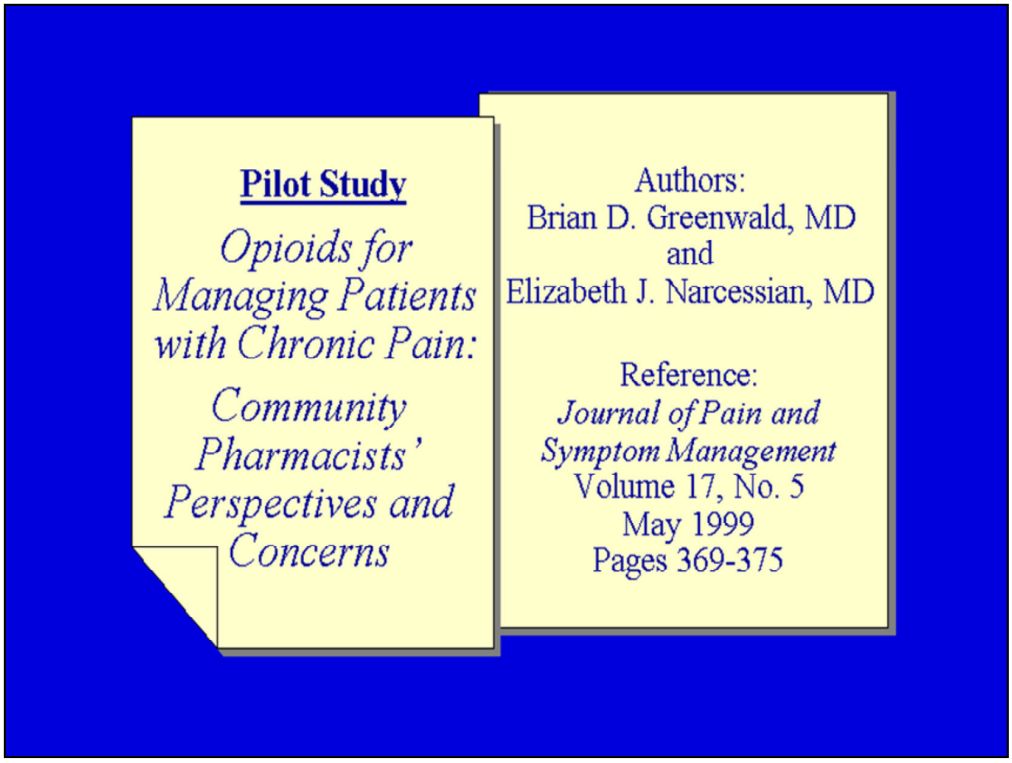
Is it ever appropriate to use opioids to treat pain in someone who has a current or previous chemical dependency?

Portenoy's Guidelines[26] Opioid Use in CNMP

A History of Substance Abuse Should be Viewed as a *Relative* Contraindication

- Personal and family medication and substance abuse histories should be thorough. Can help identify small minority that may be genetically disposed to addiction.
- Early (i.e., adolescent) experimentation with recreational drugs is not considered contraindication for maintenance opioid therapy.

26. Portenoy RK. *J Pain Symptom Manage.* 1990;5:S46-S62.

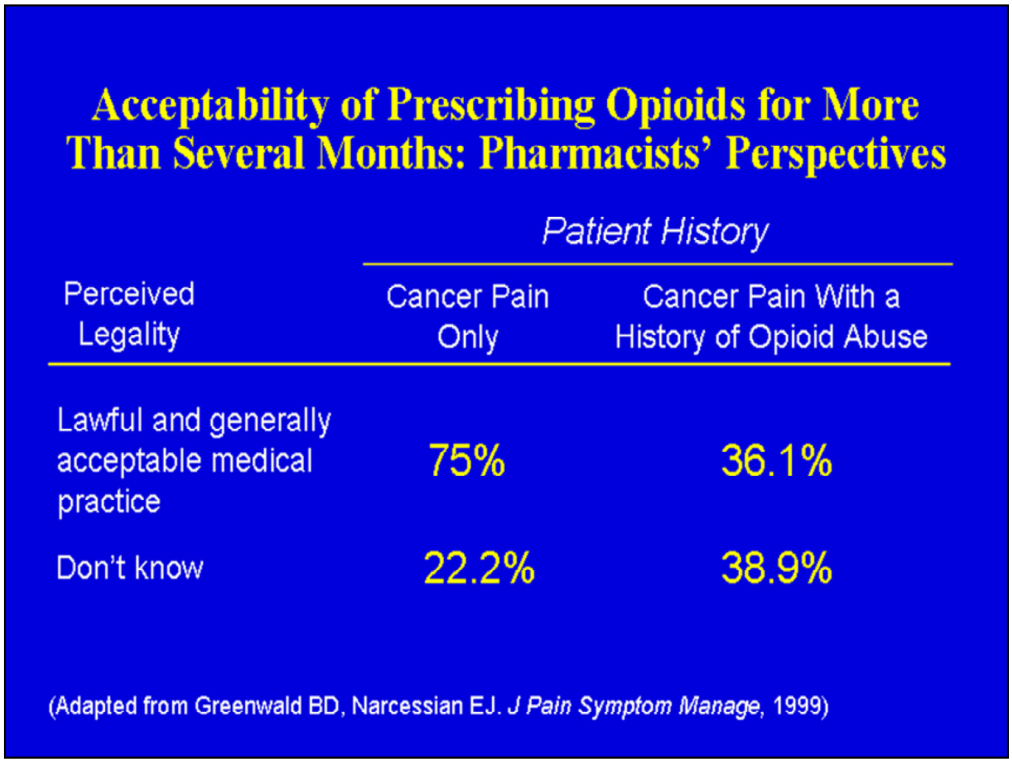


This pilot study surveyed pharmacists on issues revolving around the poor availability of opioids, and apprehension about dispensing these drugs.

Slide Reference

Greenwald BD, Narcessian EJ. Opioids for managing patients with chronic pain: community pharmacists' perspectives and

concerns. *J Pain Symptom Manage* 1999;17:369-375.



Pharmacists were surveyed regarding their opinion on the acceptability of prescribing opioids for more than several months in patients with ***cancer pain only*** and in patients with ***cancer pain and a history of opioid abuse***. The high percentage of pharmacists who responded "don't know" should be noted.

Other responses included[19]:*

Cancer pain only

•Lawful, but generally not acceptable medical practice—should be discouraged (2.8%)

•Probable violation of my standard medical practice—should be investigated (0%)

•Probable violation of federal/state controlled substance laws—should be investigated (0%)

Cancer pain with a history of opioid abuse

•Lawful, but generally not acceptable medical practice—should be discouraged (19.4%)

•Probable violation of my standard medical practice—should be investigated (13.8%)

•Probable violation of federal/state controlled substance laws—should be investigated (8.3%)

*Respondents could give more than one response.

[19]Greenwald BD, Narcessian EJ. Opioids for managing patients with chronic pain: community pharmacists' perspectives and concerns. *J Pain Symptom Manage* 1999;17:369-375.

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Greenwald BD, Narcessian EJ. Opioids for managing patients with chronic pain: community pharmacists' perspectives and

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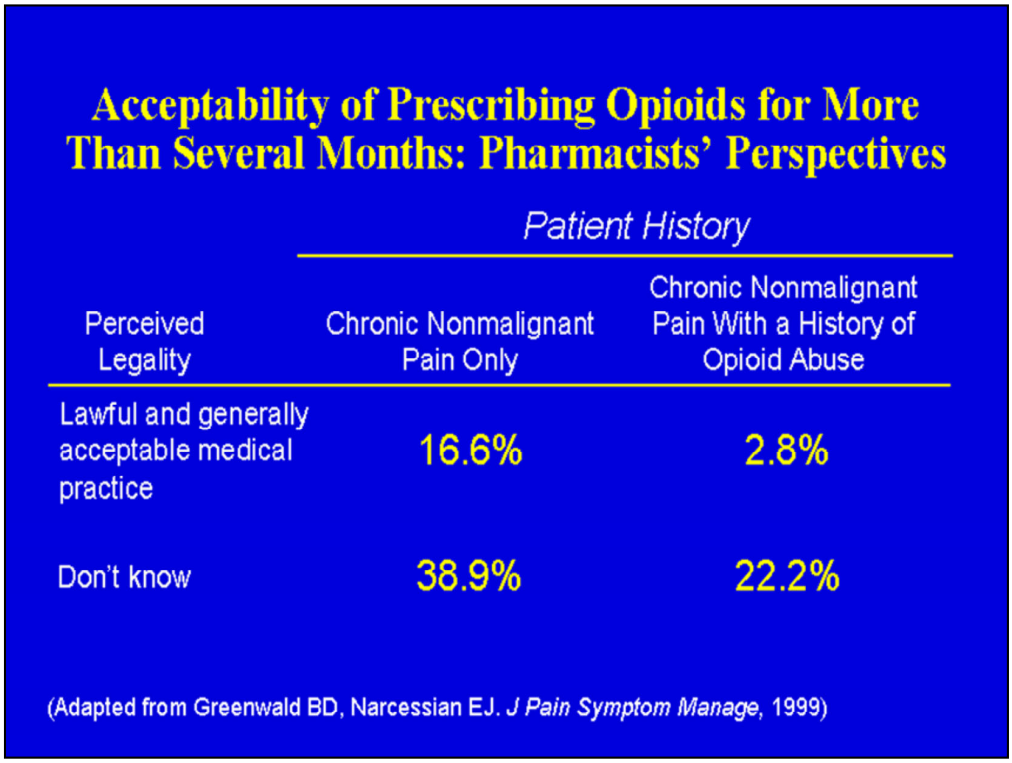

Pharmacists were surveyed regarding their opinion on the acceptability of prescribing opioids for more than several months in patients with ***chronic nonmalignant pain only*** and in patients with ***chronic nonmalignant pain and a history of opioid abuse***. The high percentage of pharmacists who responded "don't know" should be noted.

Other responses included[19]:*

Chronic nonmalignant pain only

•Lawful, but generally not acceptable medical practice—should be discouraged (47.2%)

•Probable violation of my standard medical practice—should be investigated (5.5%)

•Probable violation of federal/state controlled substance laws—should be investigated (2.8%)

Chronic nonmalignant pain with a history of opioid abuse

•Lawful, but generally not acceptable medical practice—should be discouraged (44.4%)

•Probable violation of my standard medical practice—should be investigated (36.1%)

•Probable violation of federal/state controlled substance laws—should be investigated (22.2%)

*Respondents could give more than one response.

[19]Greenwald BD, Narcessian EJ. Opioids for managing patients with chronic pain: community pharmacists' perspectives and concerns. *J Pain Symptom Manage* 1999;17:369-375.

Slide Reference

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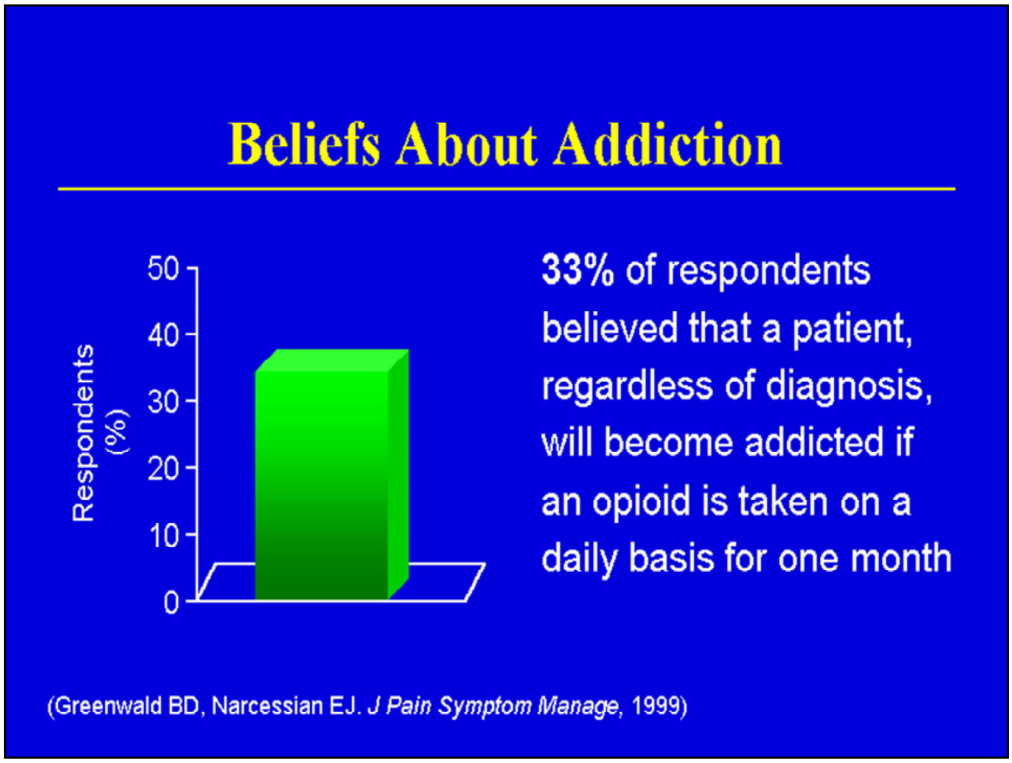

Respondents expressed the following additional concerns with prescribing practices regarding opioids[19]:

•36% believed it is illegal for a physician to prescribe methadone for pain unless certified in addiction medicine.*

•36% stated they would be resistant to fill prescriptions from a single doctor for more than one opioid.

*A physician must be certified in addiction medicine only if he or she is treating *an addict* with opioids (methadone) *for addiction.*[21]

[19]Greenwald BD, Narcessian EJ. Opioids for managing patients with chronic pain: community pharmacists' perspectives and concerns. *J Pain Symptom Manage* 1999;17:369-375.

[21]Joranson DE, Cleeland CS, Weissman DE, Gilman AM. Opioids for cancer and noncancer pain: a survey of state board members. *Fed Bulletin* 1992;79:15-49.

Slide Reference

Greenwald BD, Narcessian EJ. Opioids for managing patients with chronic pain: community pharmacists' perspectives and

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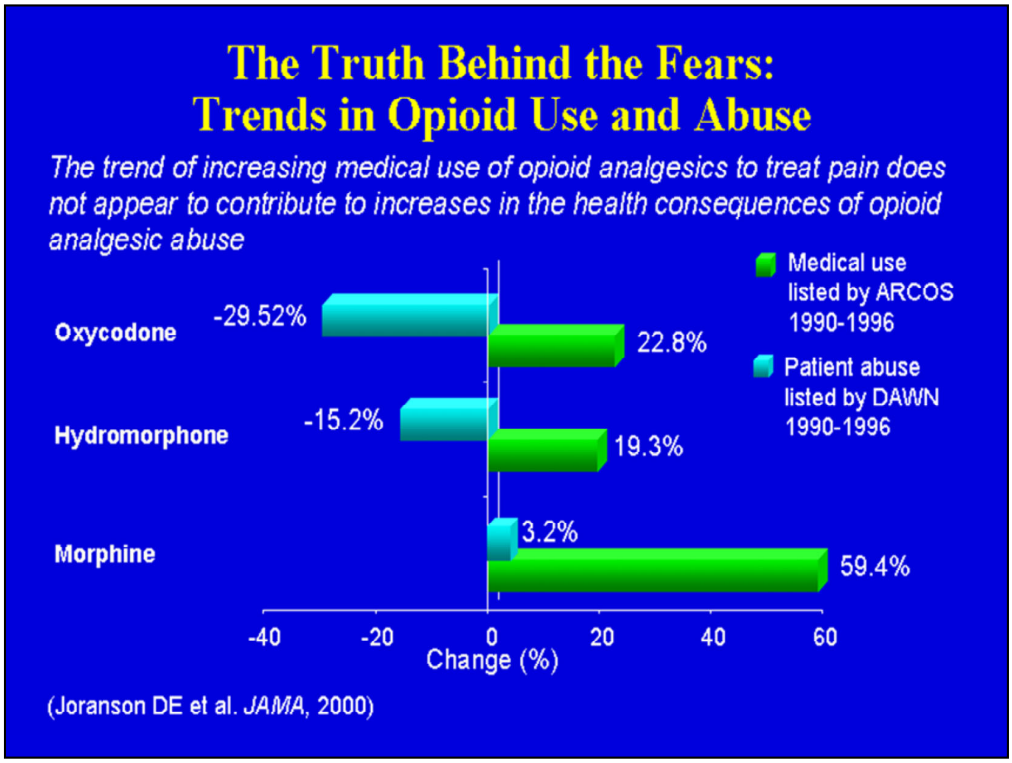
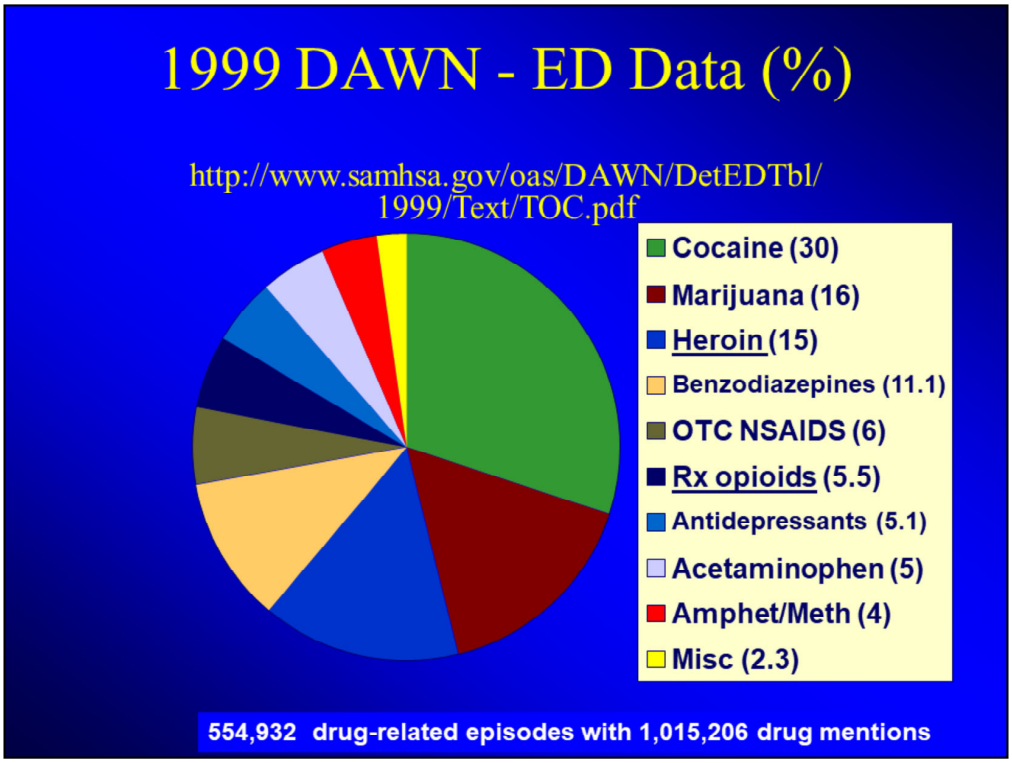


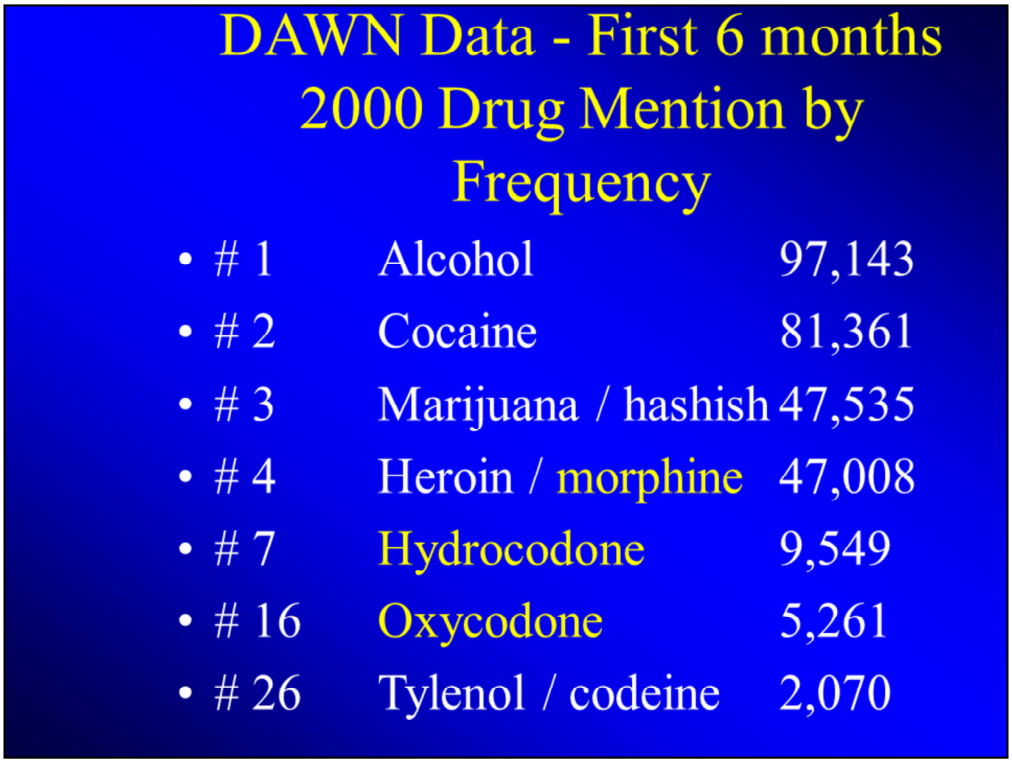
A descriptive study published in the April 5, 2000 issue of the *Journal of the American Medical Association* (*JAMA*) evaluated the trends in the medical use and abuse* of five opioid analgesics: oxycodone, hydromorphone, morphine, fentanyl, and meperidine.[26]

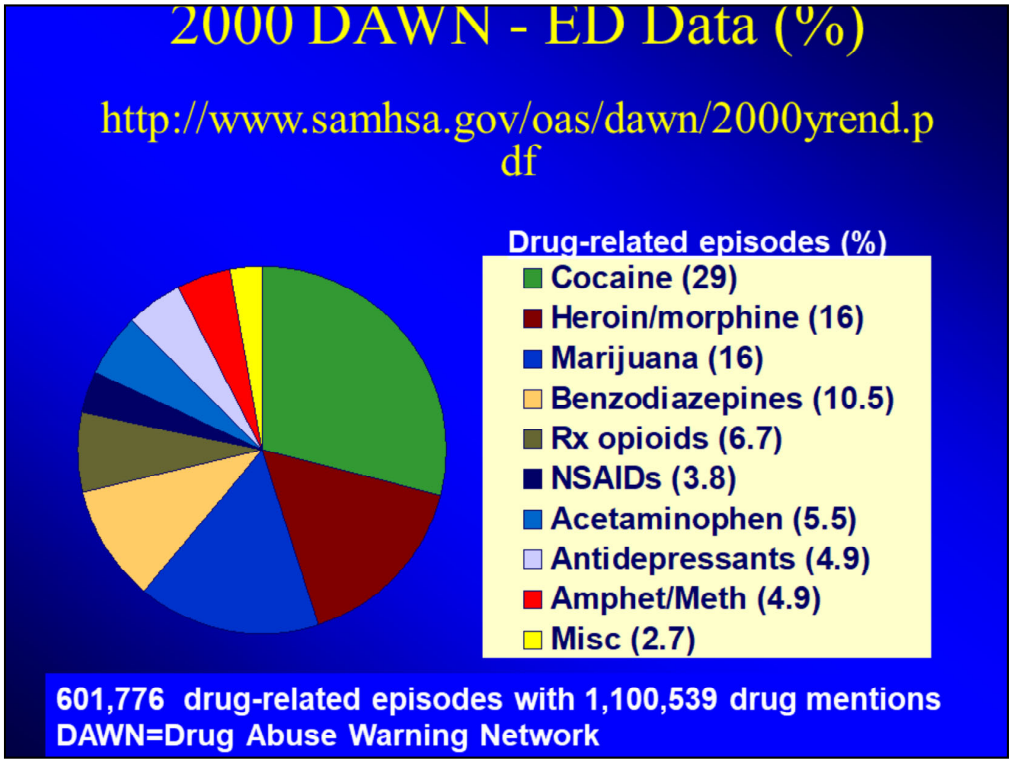
Increases in the medical use of all of the opioids were observed with the exception of meperidine.[26] During the same time period, reports of abuse (defined as the nonmedical use by patients of a substance— including prescription drugs—for psychic effect, dependence, or suicide attempt or gesture) decreased for all opioids, with the exception of morphine which increased 3%.[26]

The study concluded that "the present trend of increasing medical use of opioid analgesics to treat pain does not appear to be contributing to increases in the health consequences of opioid analgesic abuse."[26]

* Source of data
• *Abuse data:* Drug Abuse Warning Network (DAWN)
- large-scale ongoing retrospective survey of medical records used to monitor national drug abuse trends
• *Medical use data:* Automation of Reports and Consolidated Orders Systems (ARCOS)
- federal, computerized data system used to monitor the lawful distribution of controlled substances in Schedules I and II, and narcotic substances in Schedule III, from manufacturers to the retail level of


1999 DAWN - ED Data (%)
http://www.samhsa.gov/oas/DAWN/DetEDTbl/1999/Text/TOC.pdf
Cocaine (30)
Marijuana (16)
Heroin (15)
Benzodiazepines (11.1)
OTC NSAIDS (6)
Rx opioids (5.5)
Antidepressants (5.1)
Acetaminophen (5)
Amphet/Meth (4)
Misc (2.3)
554,932 drug-related episodes with 1,015,206 drug mentions


DAWN Data - First 6 months 2000 Drug Mention by Frequency
• # 1 Alcohol 97,143
• # 2 Cocaine 81,361
• # 3 Marijuana / hashish 47,535
• # 4 Heroin / morphine 47,008
• # 7 Hydrocodone 9,549
• # 16 Oxycodone 5,261
• # 26 Tylenol / codeine 2,070



The Drug Abuse Warning Network (DAWN) is maintained by the Substance Abuse and Mental Health Services Administration (SAMHSA) of the Public Health Service. DAWN is a federally-operated system that monitors more than 500 emergency departments for drug abuse trends in 21 metropolitan areas around the country.

This is the emergency department data for 2000—the most recent year for which complete data is available. Each emergency department visit is referred to as an 'episode.' There were more than six hundred thousand drug-related episodes in this sample. Up to four drugs can be mentioned as being related to the reason for each emergency department episode. More than one million drugs were mentioned. An average of 1.8 drug mentions were involved per episode.

The pie chart shows the distribution of drugs mentioned. Note that prescription opioids account for about 6.7% of all emergency department mentions. That is less than two thirds of what benzodiazepines account for, and about equal to OTC NSAIDs. Although diversion and abuse of prescription opioids is significant, they are not the only drug abuse problem.

Federal and State Controlled Substance Law

Controlled Substances Act 1970

" A prescription for a controlled substance to be effective must be issued for a legitimate medical purpose by an individual practitioner acting in the usual course of his professional practice."

"...corresponding responsibility rests with the pharmacist who fills the prescription."

21 CFR 1306.04(a)

Controlled Substances Act 1970

Allows any registrant to "administer or dispense narcotic drugs to persons with intractable pain in which no relief or cure is possible or none has been found after reasonable efforts"

21 CFR 1306.07 (c)

Drug Enforcement Administration

- What is the DEA position on prescribing controlled substances for pain experienced by:
  - someone with cancer ?
  - someone with chronic pain not due to cancer ?

Drug Enforcement Administration

"Controlled substances and, in particular, narcotic analgesics, may be used in the treatment of pain experienced by a patient with a terminal illness or a chronic disorder."

Physician's Manual: An informational outline of the Controlled Substances Act, March 1990, p 21.

Drug Enforcement Administration

"These drugs have a legitimate clinical use and the physician should not hesitate to prescribe, dispense or administer them when they are indicated for a legitimate medical purpose."

Physician's Manual: An informational outline of the Controlled Substances Act, March 1990, p 21.

Drug Enforcement Administration

"It is the position of the DEA that these controlled substances should be prescribed, dispensed or administered when there is a legitimate medical need."

Physician's Manual: An informational outline of the Controlled Substances Act, March 1990, p 21.

Summary of Federal Law

- Federal law does **not** preclude the use of opioids as analgesics for legitimate medical purposes, including treating chronic pain and treating pain in addicts.
- Federal law **does** prohibit the use of opioids to maintain an addicted state without special registration as an NTP.
- Federal law is not static (e.g., office based opioid therapy for addiction)

Slide Reference

Greenwald BD, Narcessian EJ. Opioids for managing patients with chronic pain: community pharmacists' perspectives and concerns. *J Pain Symptom Manage* 1999;17:369-375.


Discussion
and
Questions

"The first line direct strategy for controlling most pain is reassurance, maintenance of activity, and pharmacologic analgesia."[17] The three categories of analgesic medications include[6,18]:

•Non-opioid analgesics (eg, aspirin, acetaminophen, NSAIDs)

•Opioid analgesics (eg, oxycodone, morphine, hydromorphone)

•Adjuvant analgesics (eg, tricyclic antidepressants, antihistamines, benzodiazepines, steroids, anticonvulsants)

[17]Caudill MA, Holman GH, Turk D. Effective ways to manage chronic pain. *Patient Care* 1996;30:154-172.

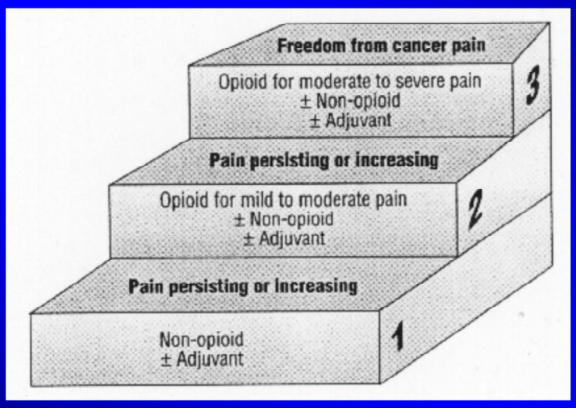
[6]American Pain Society. *Principles of Analgesic Use in the Treatment of Acute Pain and Cancer Pain.* 4th ed. Glenview, IL: American Pain Society; 1999.

[18]Portenoy RK. Current pharmacotherapy of chronic pain. *J Pain Symptom Manage* 2000;19:S16-S20.

Slide Reference

Portenoy RK. Current pharmacotherapy of chronic pain. *J Pain Symptom Manage* 2000;19:S16-S20.

The WHO Three-Step Analgesic Ladder



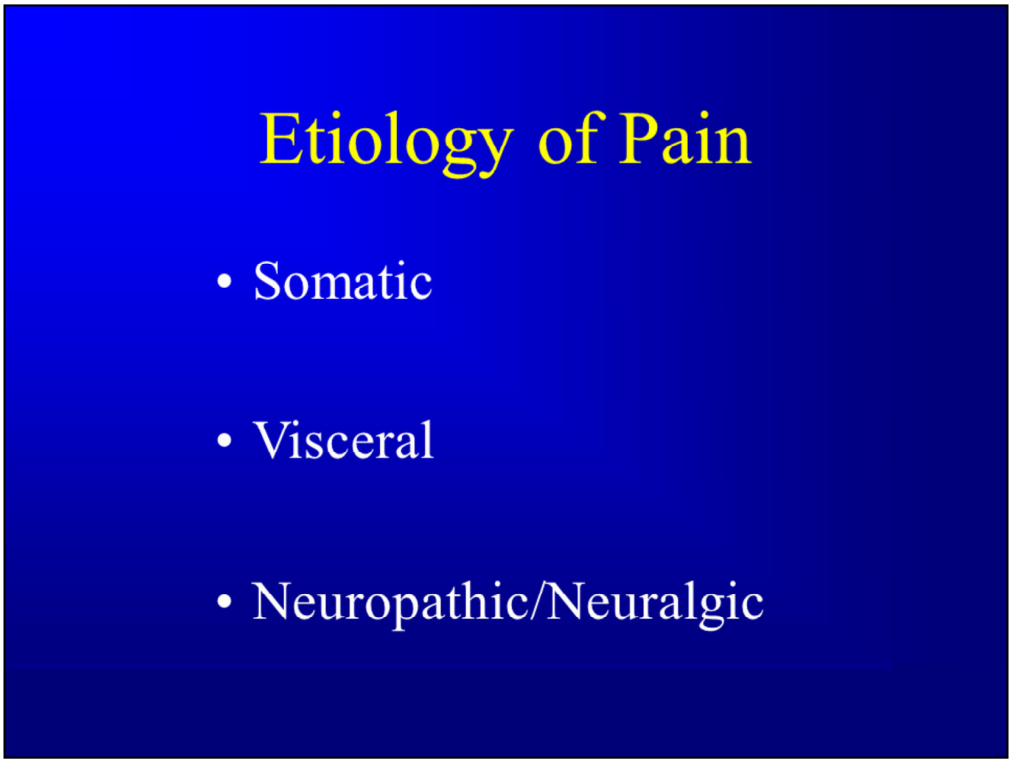
World Health Organization. Cancer Pain Relief. 1996.

Pain Assessment Scales

The more accurate the assessment of pain, the more effective the treatment

Pain Assessment

- Site
- Variation
- Intensity
- Function



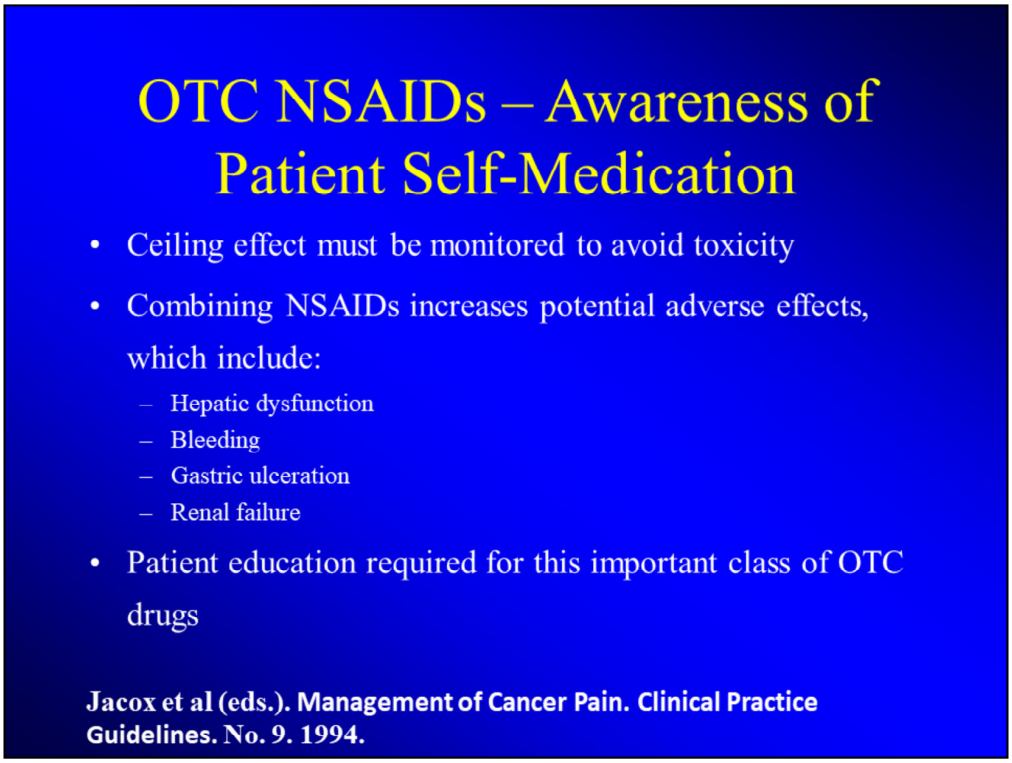
The ladder can be confusing because it only says, "+/- adjuvants" without clarifying when they may be appropriate.

Our assessment information can be helpful in determining our pharmacologic therapy.

Pharmacologic Treatment of Chronic Pain

Non-steroidal Anti-inflammatory Drugs (NSAIDs)

- Most commonly used drugs for treatment of mild to moderate pain
  - NSAIDs inhibit the enzyme cyclooxygenase (COX) thus decreasing levels of mediators that cause pain, inflammation
  - No apparent differences in efficacy among NSAIDs[21]



Acetylated salicylates

Example: Aspirin

irreversibly inhibits cyclooxygenase

inhibits platelet aggregation for life of platelet

Non-acetylated salicylates

Example:

choline/Magnesium trisalicylate

reversibly inhibits cyclooxygenase (COX)

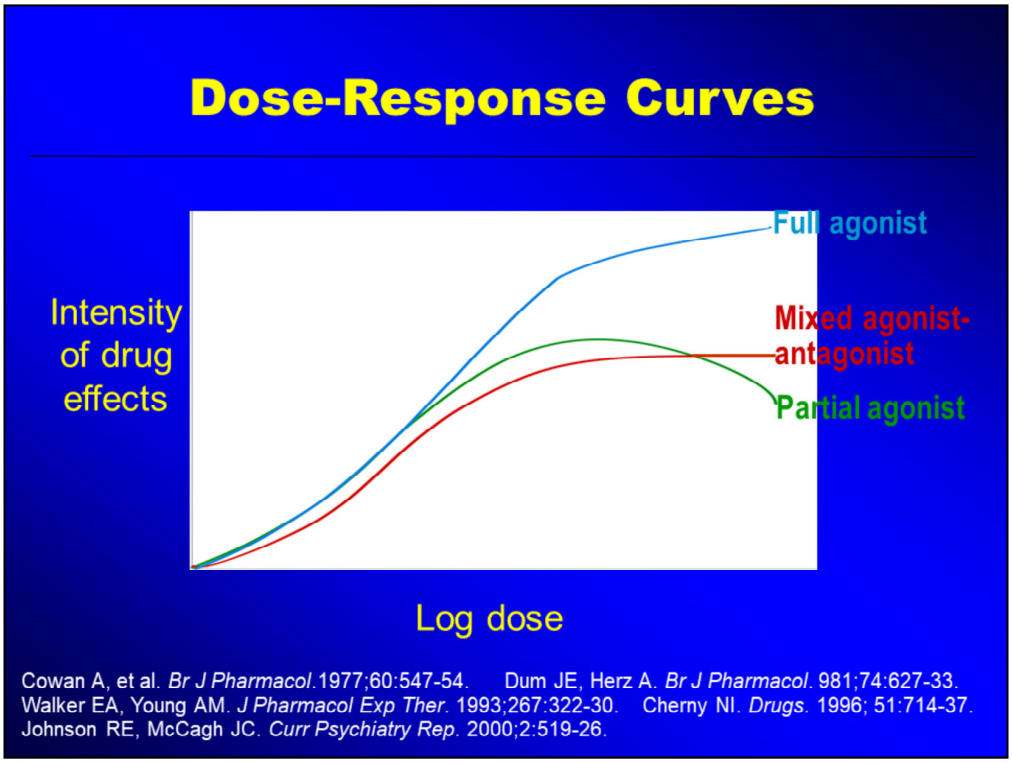
minimal to no inhibition of platelet aggregation

Primarily inhibit COX-2

Examples

celecoxib

rofecoxib



Full agonist opioids have no apparent ceiling to analgesia or side effects. As the dose is raised, these effects increases in a log-linear function.[1] Animal studies have demonstrated that buprenorphine has a bell-shaped dose-response curve for analgesia and side effects.[2,3,4] As a result, there is a ceiling to the physiologic (including respiratory depression), subjective, and behavioral effects of buprenorphine. Agonist-antagonist opioids also have a ceiling to their effects, which is lower than the maximal effect produced by a full agonist.[1,4,6]

1. Cherny NI. Opioid Analgesics. Comparative Features and Prescribing Guidelines. *Drugs*. 1996;51:714-37.

2. Cowan A, et al. Agonist and antagonist properties of buprenorphine, a new antinociceptive agent. *Br J Pharmacol*.1977;60:547-54.

3. Dum JE, Herz A. In vivo receptor binding of the opiate partial agonist, buprenorphine, correlated with its agonistic and antagonistic actions. *Br J Pharmacol*. 1981;74:627-33.

4. Johnson RE, McCagh JC. Buprenorphine and naloxone for heroin dependence. *Curr Psychiatry Rep*. 2000;2:519-26.

5. Budd K. Experience with partial agonists in the treatment of cancer pain. *Opioids in The Treatment of Cancer Pain.* 1990: *Royal Society of Medicine Services Congress & Symposium* Series No. 146.51-5.

6. Walker EA, Young AM. Discriminative-stimulus effects of the low efficacy mu agonist nalbuphine. *J Pharmacol Exp Ther*. 1993;267:322-30.

Pharmacologic Treatment of Chronic Pain

Opioid Analgesics

- Opioids are among the most useful, versatile pharmacologic tools to treat pain
  - Morphine
  - Oxycodone
  - Hydrocodone
  - Hydromorphone
- Opioids act spinally, supraspinally, and at peripheral sites of tissue injury[23]

Side Effects of Chronic Opioid Therapy

- Opioids remarkably well tolerated in chronic use
- Side effects most common when opioid-naïve patients begin therapy
- Tolerance to cognitive effects (i.e., drowsiness) typically occurs within a few days of initiating therapy, or escalating the dose[15]
- Tolerance to centrally mediated effects (i.e., respiratory depression) may be seen within 5 to 7 days of continuous administration of regularly scheduled opioids[16]
- Tolerance *does not* develop to opioid-induced constipation; it should be anticipated and prevented whenever possible[15]

15. Levy MH. *Semin Oncol.* 1985;12(4):394-410.
16. Walsh TD, Baxter R, Bowman K, Leber B. *Pain.* 1981;suppl 1:S39, Abstract.

Guidelines for Opioid Dose Titration

- The optimal analgesic dose varies widely among patients with cancer and non-cancer pain
- Optimal management of cancer pain requires aggressive upward dose titration

(APS 1999) (Levy MH. *N Engl J Med*, 1996)

Tolerance

- *"Tolerance is a physiologic state resulting from regular use of a drug in which an increased dose is needed to produce the same effect or a reduced effect is observed with a constant dose."*[8]
- Analgesic tolerance is the need to increase the dose of opioid to achieve the same desired level of analgesia.
- Tolerance to opioid analgesia typically *does not* occur once an effective dose is identified and administered regularly.
- The need to gradually raise the initial opioid dose does not reflect tolerance; it is the process of titrating to response.

8. *Model Guidelines for the Use of Controlled Substances for the Treatment of Pain.* Federation of State Medical Boards of the United States, Inc. May, 1998, Euless, Texas.

Pseudotolerance

When a stable opioid dose ceases to be effective, pseudotolerance may be a factor. The need to increase a stable dose may be due to[25]

- Increasing or new pathology
- Increased physical activity after pain diminishes
- Change in medication formulation, brand, or supplier
- Noncompliance
- Other nonpharmacologic factors

Opioid Metabolism

- Consider metabolic pathway when selecting a specific drug
- Opioid metabolites may cause neurotoxicity[28] and displace parent compound from opioid receptor sites
- Patients at risk include [28]
  - Those with impaired renal function (e.g., most elderly)
  - Those receiving high-dose or long-term opioid therapy

Opioid Metabolism

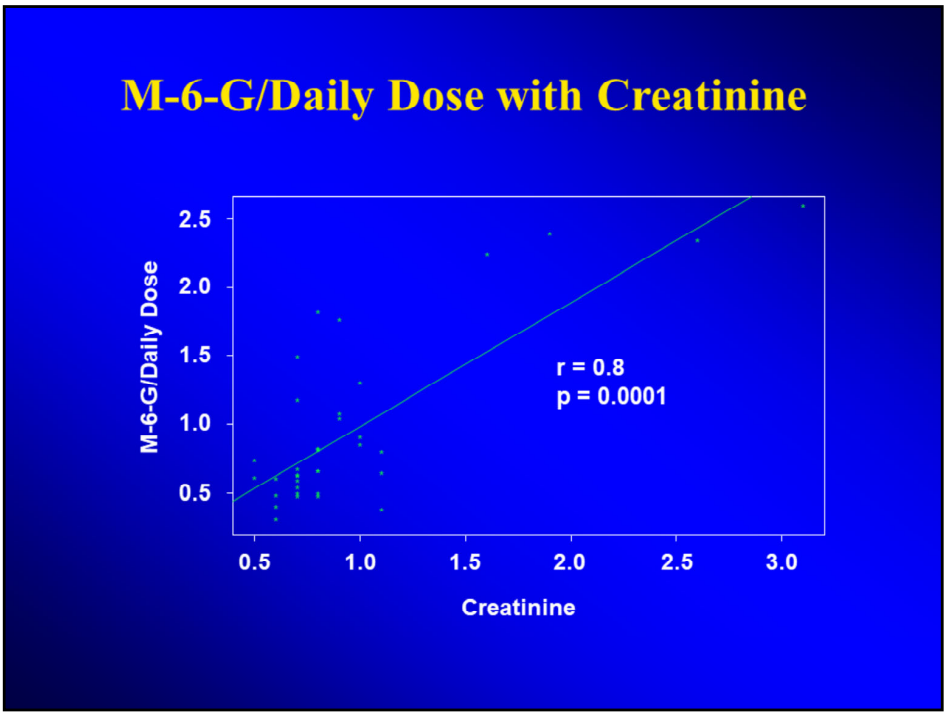
- Use special caution with meperidine [28]
- Accumulation of metabolite normeperidine, causes neurotoxicity
- Particularly dangerous for elderly, patients with poor renal function
- Use should be limited to 1 to 2 days for acute pain

Opioid Metabolism

- M3G accounts for about 50% of parent drug excreted[29]
  - Appears to be associated with hyperalgesia, myoclonus, other neuro-excitatory toxicities[28]
- M6G accounts for 5% of parent drug excreted [29]
  - Has analgesic properties; may be significantly more potent than morphine
- Accumulation of M6G and M3G, due to poor renal status, predisposes patients to toxicity, poor pain control[28]

28. Pereira J, Bruera E. *J Pharm Care Pain and Symptom Control*. 1997;5(4):3-29.

29. Forman WB. *Clin Geriatr Med*. 1996:12:489-500.

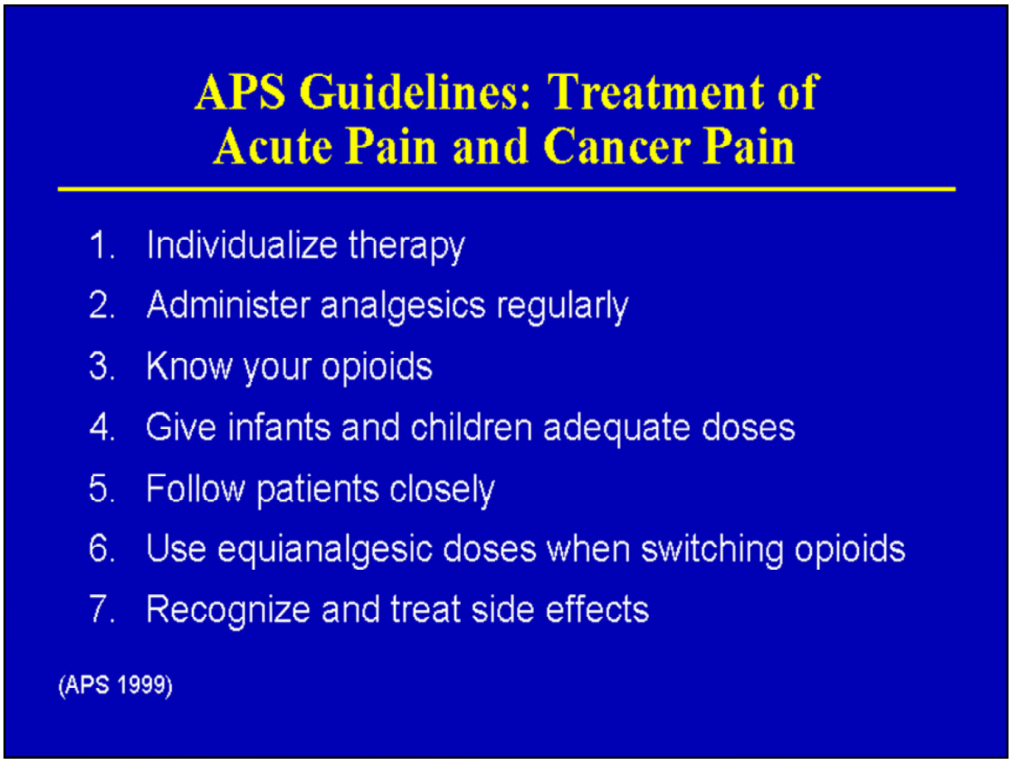


Slide 28

- In this study, we also examined oxycodone and its metabolites and morphine and its metabolites as a function of standard clinical chemistry measures of renal and hepatic function.* We looked for significant relationships between plasma opioid concentrations and measures of kidney or liver function.
- The only significant relationship we found was between morphine-6-glucuronide and renal function tests.
- This graph illustrates the relationship between morphine-6-glucuronide concentrations and serum creatinine concentrations.

_____

*If asked: BUN, serum creatinine, AST (SGOT), ALT (SGPT), and total bilirubin.


APS Guidelines: Treatment of Acute Pain and Cancer Pain
1. Individualize therapy
2. Administer analgesics regularly
3. Know your opioids
4. Give infants and children adequate doses
5. Follow patients closely
6. Use equianalgesic doses when switching opioids
7. Recognize and treat side effects
(APS 1999)

APS Guidelines: Treatment of Acute Pain and Cancer Pain

(cont'd)

8. Be aware of hazards of meperidine and mixed agonist-antagonists
9. Do not use placebos to assess pain
10. Treat tolerance
11. Be aware of the development of physical dependence and prevent withdrawal
12. Do not confuse addiction with physical dependence or tolerance
13. Be alert to the psychological state of patients

(APS 1999)

Because the AGS recognizes that older patients are at significant risk for undertreatment of their pain, they published Panel recommendations regarding this issue.

Pain in the Elderly – Nonopioid Analgesic Treatment:

- Avoid NSAIDs in abnormal renal function, bleeding diathesis, or a history of peptic ulcer[1]
- Avoid the use of more than one NSAID at a time
- Anticipate ceiling dose limitations
- GI-protective drugs do not prevent renal impairment and other interactions

Reference: 1. American Geriatrics Society Panel on Chronic Pain in Older Persons. *J Am Geriatr Soc.* 1998;46:635-651.

Pain in the Elderly – Opioid Pharmacologic Treatment: (cont'd.)

- Chronic opioid therapy, low-dose corticosteroid therapy, or other adjunctive drug therapies may have fewer life-threatening risks than long-term daily use of high-dose NSAIDs[1]

Reference: 1. American Geriatrics Society Panel on Chronic Pain in Older Persons. *J Am Geriatr Soc.* 1998;46:635-651.

Pain in the Elderly – Opioid Pharmacologic Treatment:

- Opioid analgesics can relieve moderate to severe pain, especially nociceptive pain[1]
- Fears of drug dependency and addiction do not justify the failure to relieve pain
- For occasional chronic recurrent or noncontinuous pain not controlled by NSAIDs, prescribe opioid analgesics PRN

Reference: 1. American Geriatrics Society Panel on Chronic Pain in Older Persons. *J Am Geriatr Soc.* 1998;46:635-651.

Pain in the Elderly – Around-the-Clock Dosing

For continuous pain, medications are best given on a regular around-the-clock basis[1]

- Additional doses may be required before activities known to exacerbate pain

Reference: 1. American Geriatrics Society Panel on Chronic Pain in Older Persons. *J Am Geriatr Soc.* 1998;46:635-651.

Pain in the Elderly – Treating Side Effects:

- Prevent constipation with a prophylactic bowel regimen[1]
- Encourage adequate fluid intake
- Prescribe a bowel stimulant or motility agent, if necessary
- Treat mild sedation, severe nausea, severe pruritus, and myoclonus

Reference: 1. American Geriatrics Society Panel on Chronic Pain in Older Persons. *J Am Geriatr Soc.* 1998;46:635-651.

Pain in the Elderly – Opioid Pharmacologic Treatment:

- "Start low and go slow"[1]
- Elderly patients may be more sensitive to opioids, experiencing higher peak effect and longer duration of pain relief[2]
- Age-adjusted dosing recommendations are not available
- PCA should be monitored especially closely in the elderly[3]

References: 1. American Geriatrics Society Panel on Chronic Pain in Older Persons. *J Am Geriatr Soc.* 1998;46:635-651. 2. Kaiko RF. *Clin Pharmacol Ther.* 1980;28:823-826. 3. Ferrell BR, Cronin Nash C, Warfield C. *J Pain Symptom Manage.* 1992;7:149-154.

Pain in the Elderly – Around-the-Clock Dosing (cont'd.)

- Drug regimens should be as simple as possible, with the focus on decreased pain, improved function, and improved mood and sleep – not decreased drug dose[1]
- All medication management must be tailored to the individual patient

Reference: 1. American Geriatrics Society Panel on Chronic Pain in Older Persons. *J Am Geriatr Soc.* 1998;46:635-651.

Pain in the Elderly – Adjuvant Analgesic Treatment

- Adjuvant analgesic drugs may reduce pain in certain intractable pain syndromes[1]
- The use of these drugs increases the potential for adverse drug reactions, particularly in older patients[1]

Reference: 1. American Geriatrics Society Panel on Chronic Pain in Older Persons. *J Am Geriatr Soc.* 1998;46:635-651.

Consider things that can complicate therapy…

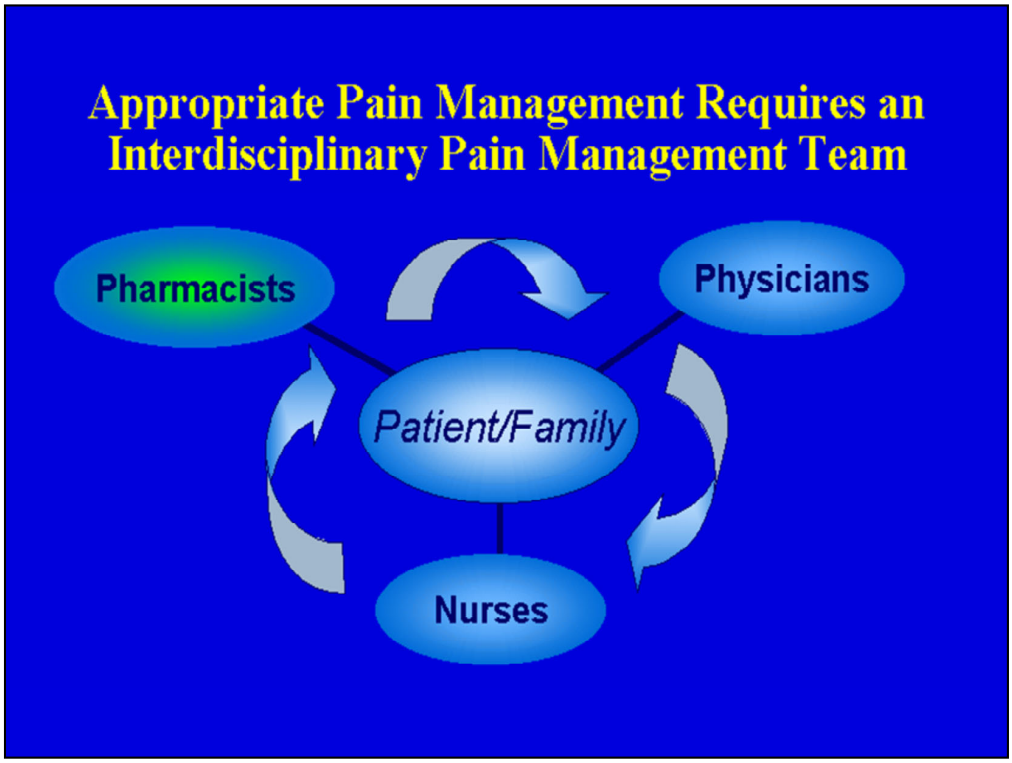
poly-pharmacy

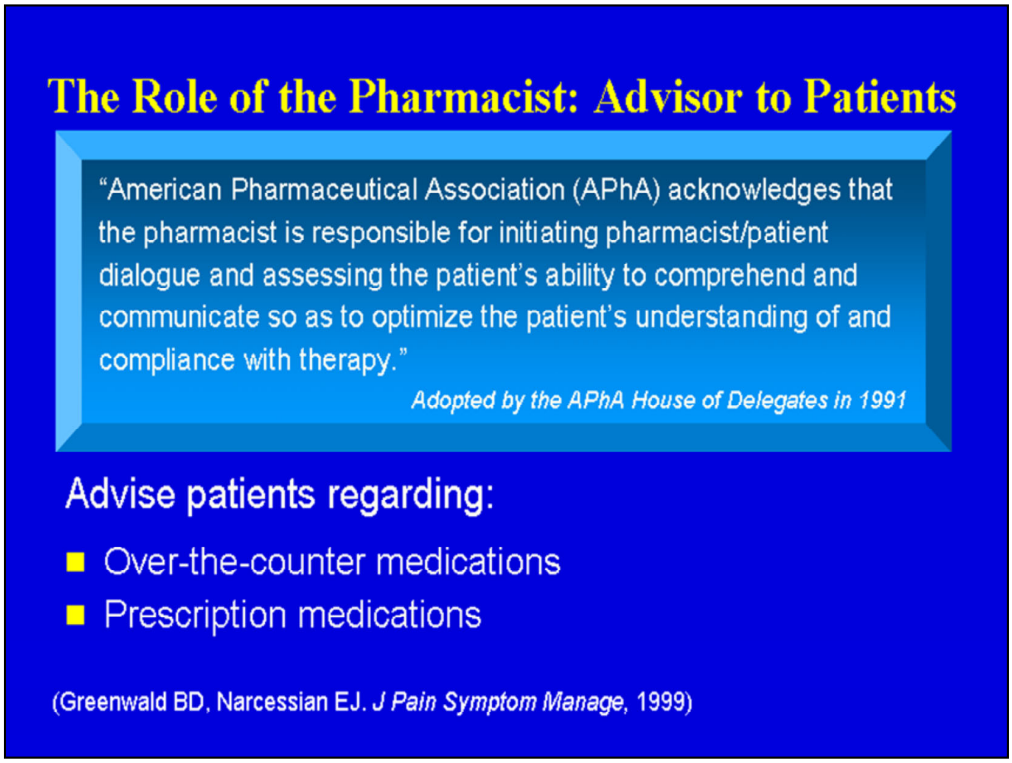
phys dep?

tolerance?

How do you evaluate if a

medication profile represents poly-pharmacy or appropriate multi-modality? How many **different** mechanisms of action (or durations of therapy – short acting + long acting opioids) are represented within the medication profile?


Appropriate Pain Management Requires an Interdisciplinary Pain Management Team
Pharmacists
Physicians
Patient/Family
Nurses



As advisors to patients about medications, pharmacists take on a crucial role in impacting the outcome of a patient's pharmacotherapy.[19] A pharmacist's inadequate knowledge of issues pertinent to the pharmacological management of pain may result in adverse consequences for the patient.[19]

[19]Greenwald BD, Narcessian EJ. Opioids for managing patients with chronic pain: community pharmacists' perspectives and concerns. *J Pain Symptom Manage* 1999;17:369-375.

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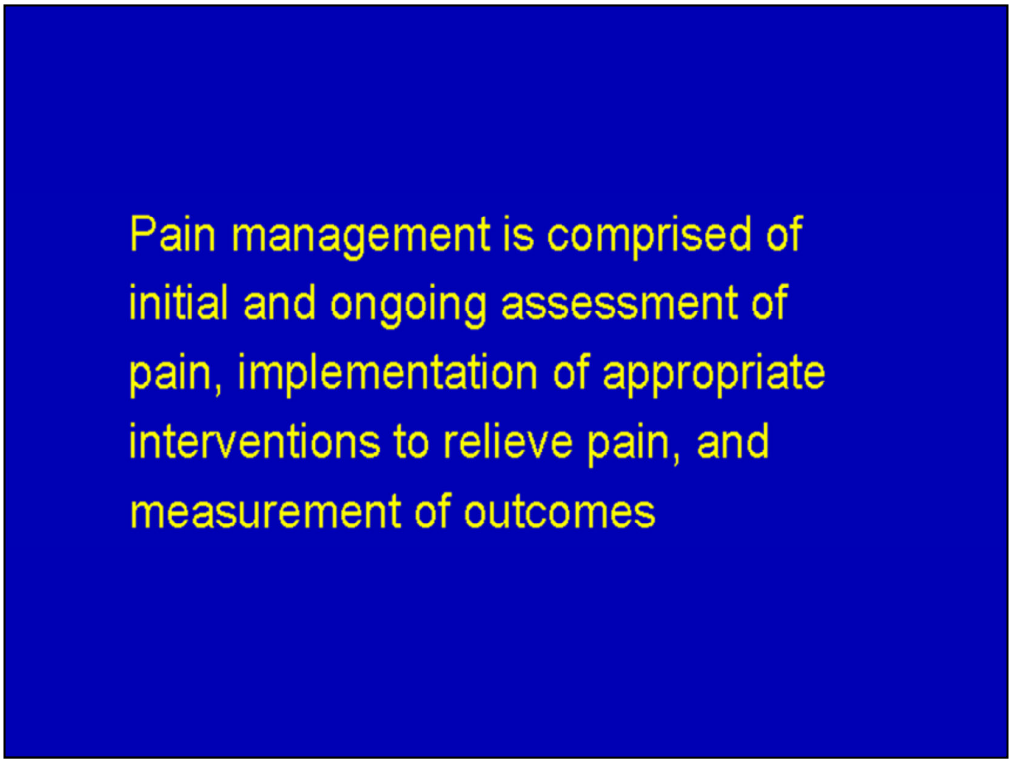
Greenwald BD, Narcessian EJ. Opioids for managing patients with chronic pain: community pharmacists' perspectives and concerns.

J Pain Symptom Manage 1999;17:369-375.


Pain management is comprised of initial and ongoing assessment of pain, implementation of appropriate interventions to relieve pain, and measurement of outcomes


Discussion
and
Questions

Produced Natively

What concerns do you have?

Legit script

Legit doctor

Legit patient

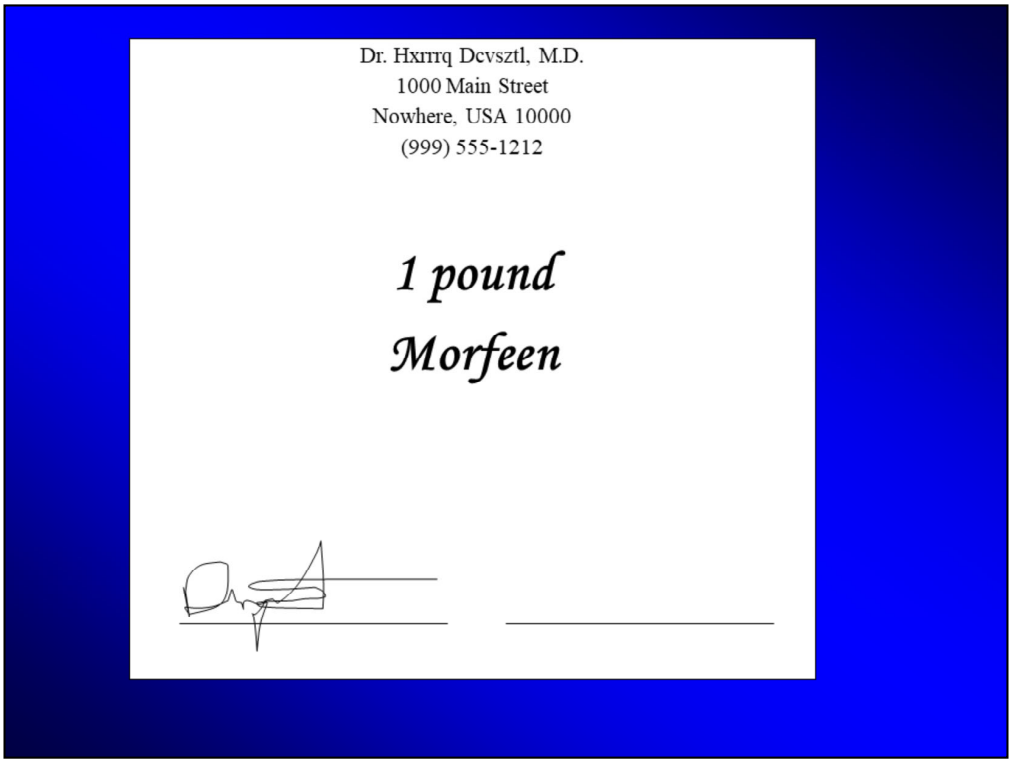
Drug choice

Drug dose

Evokes a lot of emotion:

friend / family with: chemical dependency

pain


Dr. Hxrrrq Dcvsztl, M.D.
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Example 2

- A nurse stops a physician in the hospital and asks for a small amount of a prescription drug and the physician writes the prescription without a proper H&P and documentation

Example 2

- A nurse stops a physician in the hospital and asks for a small amount of a prescription drug and the physician writes the prescription without a proper H&P and documentation
  - medical experts would testify that no physician-patient relationship existed
  - therefore, this was not legitimate medical purpose

The tenets of legal prescribing

- A legal prescription for a controlled substance must be:
  - issued for a legitimate medical purpose
  - by an individual practitioner acting in the usual course of their professional practice
  - documented in the medical records

Drug Scams

- Practitioner prescribes for deceased patients and then picks up medication for personal abuse
- Abuser posing as a pharmacist or regulator calls receptionist to obtain DEA numbers of all the prescribers in the practice
- Scams are only limited by the imagination of the drug seeker

Example of patient filling too early or at multiple pharmacies.

DIFFERENTIAL DIAGNOSIS:

Abuse

Chemical Dependence

Poor pain control

Addiction

Addiction is a primary, chronic, neurobiologic disease, with genetic, psychosocial, and environmental factors influencing its development and manifestations.

It is characterized by behaviors that include one or more of the following: impaired control over drug use, compulsive use, continued use despite harm, and craving.

Approved by the Boards of Directors of the AAPM, APS, and ASAM, February 2001

Pseudoaddiction

- Addicts normally exhibit profound "drug-seeking" behavior.
- "Drug-seeking" behavior does not always indicate abuse.
- It may indicate that a patient is an appropriate opioid candidate but is not receiving a dose sufficient to maintain lifestyle and functional level.
- Oncology setting: "Drug-seeking" behavior to obtain effective pain relief has been referred to as a "pseudoaddiction."[23]
- The phenomenon of "pseudoaddiction" has been recognized by The American Society of Addiction Medicine.[24]

23. Weissman DE, Haddox JD. *Pain.* 1989;36:363-366.
24. American Society of Addiction Medicine. *Public Policy Statement on Definitions Related to the Use of Opioids in Pain Treatment.1997.*

Pseudoaddiction

- Pseudoaddiction: Appropriate drug-seeking behavior for the purpose of pain relief, not for abuse.
  - Quickly differentiated from true abuse when an appropriate increase in dose stops the behavior.
- The potential for opioid abuse, while small, exists nonetheless, and all clinicians must be aware of the warning signs.

Physical Dependence

"Physical dependence on a controlled substance is a physiologic state of neuro-adaptation which is characterized by the emergence of a withdrawal syndrome if drug use is stopped or decreased abruptly, or if an antagonist is administered."

Physical dependence is an expected result of opioid use and, by itself, does not equate with addiction.

(Federation of State Medical Boards of the United States, Inc. *Model Guidelines for the Use of Controlled Substances for the Treatment of Pain.* Euless, TX; 1998)

Tolerance

- *"Tolerance is a physiologic state resulting from regular use of a drug in which an increased dose is needed to produce the same effect or a reduced effect is observed with a constant dose."*[8]
- Analgesic tolerance is the need to increase the dose of opioid to achieve the same desired level of analgesia.
- Tolerance to opioid analgesia typically *does not* occur once an effective dose is identified and administered regularly.
- The need to gradually raise the initial opioid dose does not reflect tolerance; it is the process of titrating to response.

8. *Model Guidelines for the Use of Controlled Substances for the Treatment of Pain.* Federation of State Medical Boards of the United States, Inc. May, 1998, Euless, Texas.

Drug Seeking Behavior

- Wants appointment toward end of office hours or telephones/arrives after regular business hours
- Insists on being seen immediately or demands immediate action. Says they are in a hurry to catch a plane, or late for a business meeting

Drug Seeking Behavior

- Not interested in having physical examination or undergoing diagnostic tests
- Unwilling to give permission to obtain past medical records
- Unable to recall hospital or clinic where past records are kept, or states they are out of business or burned down
- Unwilling or unable to give names of past health care professionals

Drug Seeking Behavior

- Claims to be from out of town and to have lost prescription, forgotten to pack medication or says that it was stolen
- Exaggerates or feigns medical problems
  - Complains of renal colic (pricks finger to add blood to urine specimen)
  - Complains of migraine, tic or toothache
- Recites textbook symptoms or gives very vague medical history

Besides hurting themselves...

Pain is a major, yet largely avoidable, public health problem.[1] In most patients with chronic painful conditions (eg, cancer, arthritis, back disorders, headache), usually it is the pain, not the underlying pathology, that limits their ability to function and lead a productive life.[2]

[1]Joint Commission Focuses on Pain Management [press release]. Oakbrook Terrace, Ill: Aug 3, 1999.

[2]Bonica JJ. General considerations of chronic pain. In: *The Management of Pain*. 2nd ed. Philadelphia: Lea & Febiger; 1990:180-195.

Slide References

Greenwald BD, Narcessian EJ. Opioids for managing patients with chronic pain: community pharmacists' perspectives and concerns. *J Pain Symptom Manage* 1999;17:369-375.

Bonica JJ. General considerations of chronic pain. In: *The Management of Pain*. 2nd ed. Philadelphia: Lea & Febiger; 1990:180-195.

Possible Adverse Effects of Undertreated Pain

Physiological

Increased catabolic demands lead to

- Muscle breakdown
- Poor healing
- Weakness

Impaired respiratory effort increases

- Risk of atelectasis

Impaired limb movement increases

- Risk of thromboembolic events

Other potential physiological consequences

- Water retention
- Inhibited GI motility
- Hypertension, tachycardia, tachypnea (acute)

Adapted from AHCPR Guidelines, 1992,[11] 1994[12]

Possible Adverse Effects of Undertreated Pain

Psychological

Negative emotions including

- Anxiety
- Depression

Other psychological effects

- Sleep deprivation
- Existential suffering

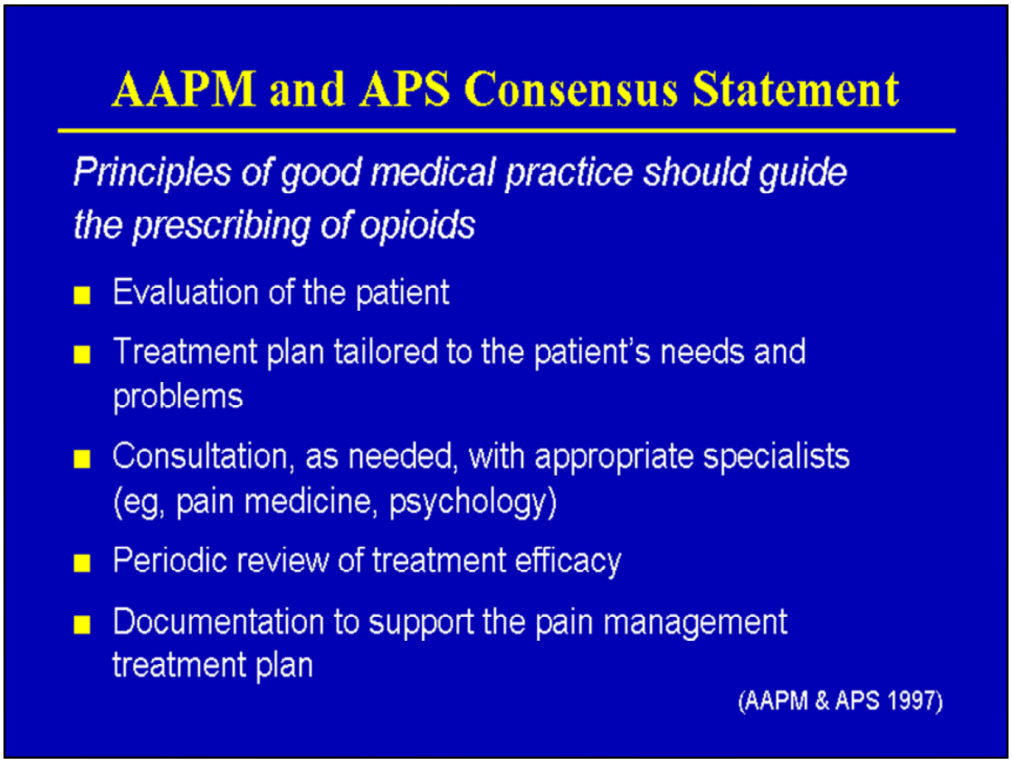
Immunological

Impaired immune response

- Decreased natural killer (NK) cells

Adapted from AHCPR Guidelines, 1992,[11] 1994[12]

Paradigm Shift in
Pain Management



Chronic pain is often inadequately treated

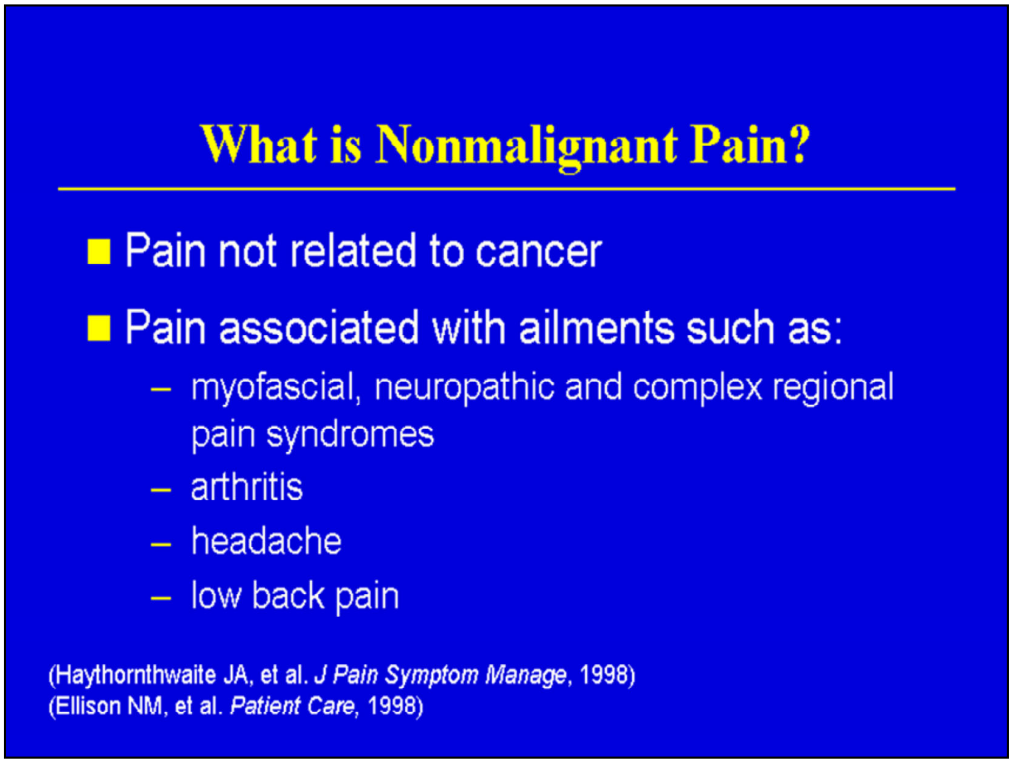
Using opioids for chronic pain is legitimate medical practice

Concerns regarding addiction, tolerance, and respiratory depression lead to underutilization

Accepted principles for opioid use should be promulgated

Principles of good medical practice should guide prescribing

Adverse events can usually be managed, or diminish with use



Over 30 million Americans suffer from chronic pain of a nonmalignant origin.[8]

[8]Holmquist GL. The appropriate use of opioids in the management of chronic pain: a pharmacist's perspective. *Pharmacy Times* 1999;29:3-11.

Slide References

Haythornthwaite JA, Menefee LA, Quatrano-Piacentini AL, Pappagallo M. Outcome of chronic opioid therapy for non-cancer pain. *J Pain Symptom Manage* 1998;15:185-194.

Ellison NM, Lipman AG, Patt RB, Portenoy RK. Opioid analgesia: an essential tool in chronic pain. *Patient Care* 1998;32:2-11.

Interdisciplinary Team Members

Physicians

Preferably board certified by American Board of Pain Medicine or of Anesthesiologists; have earned the American Board of Anesthesiology qualification in pain

- Medical management
- Most common professionals:
  - Anesthesiologists
  - Neurologists
  - Physiatrists
  - Psychiatrists

Interdisciplinary Team Members

Mental health professionals

- Cognitive behavioral therapy
  - Addresses learned pain behaviors
- Management of psychological disorders and somatization
- Most common professionals
  - Psychologists with advanced training in behavioral medicine
  - Sometimes social workers

Interdisciplinary Team Members

Nurses

- Patient education
- Case management

Rehabilitation specialists

- Physical therapy
- Occupational therapy
- Recreational therapy
- Vocational counseling

Interdisciplinary Team Members

Pharmacists

- Obtain detailed medication histories
- Monitor and manage drug therapy (pharmaceutical care plan)
- Manage cessation of ineffective medications
- Provide patient education
- Provide drug information/education to team members

These multidisciplinary teams care for some of the most complicated patients.

They have rules, contracts, urine tox screens, etc.

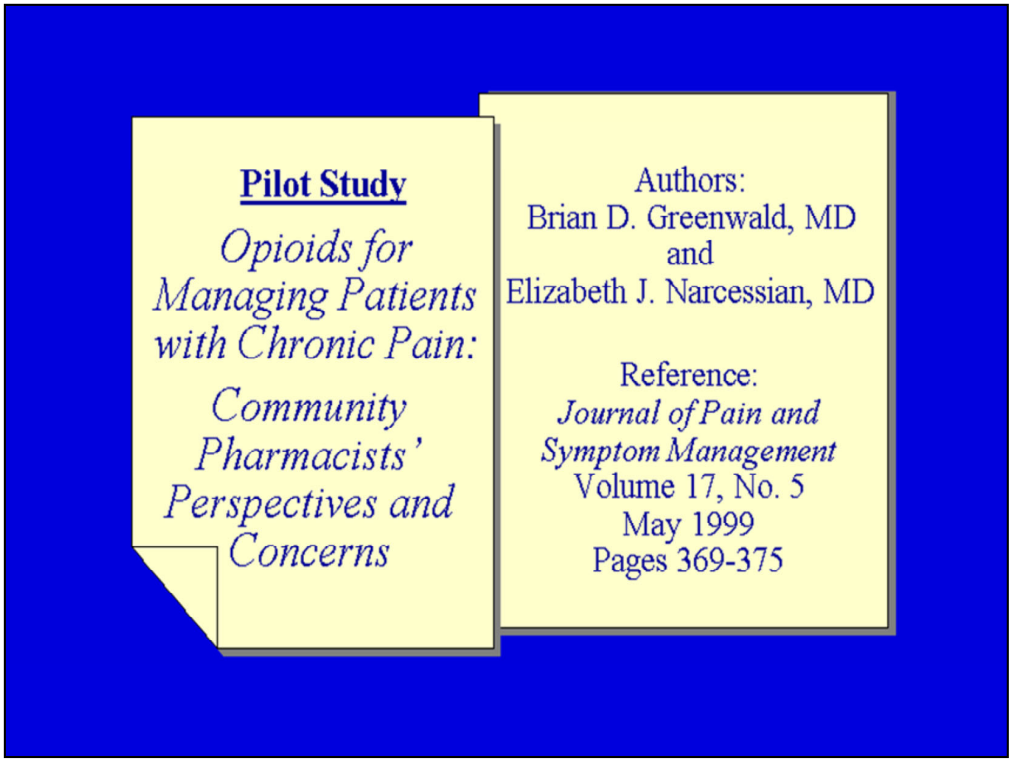
Is it every appropriate to use opioids to treat pain in someone who has a current or previous chemical dependency?

Portenoy's Guidelines[26] Opioid Use in CNMP

A History of Substance Abuse Should be Viewed as a *Relative* Contraindication

- Personal and family medication and substance abuse histories should be thorough. Can help identify small minority that may be genetically disposed to addiction.
- Early (i.e., adolescent) experimentation with recreational drugs is not considered contraindication for maintenance opioid therapy.

26. Portenoy RK. *J Pain Symptom Manage.* 1990;5:S46-S62.



This pilot study surveyed pharmacists on issues revolving around the poor availability of opioids, and apprehension about dispensing these drugs.

Slide Reference

Greenwald BD, Narcessian EJ. Opioids for managing patients with chronic pain: community pharmacists' perspectives and

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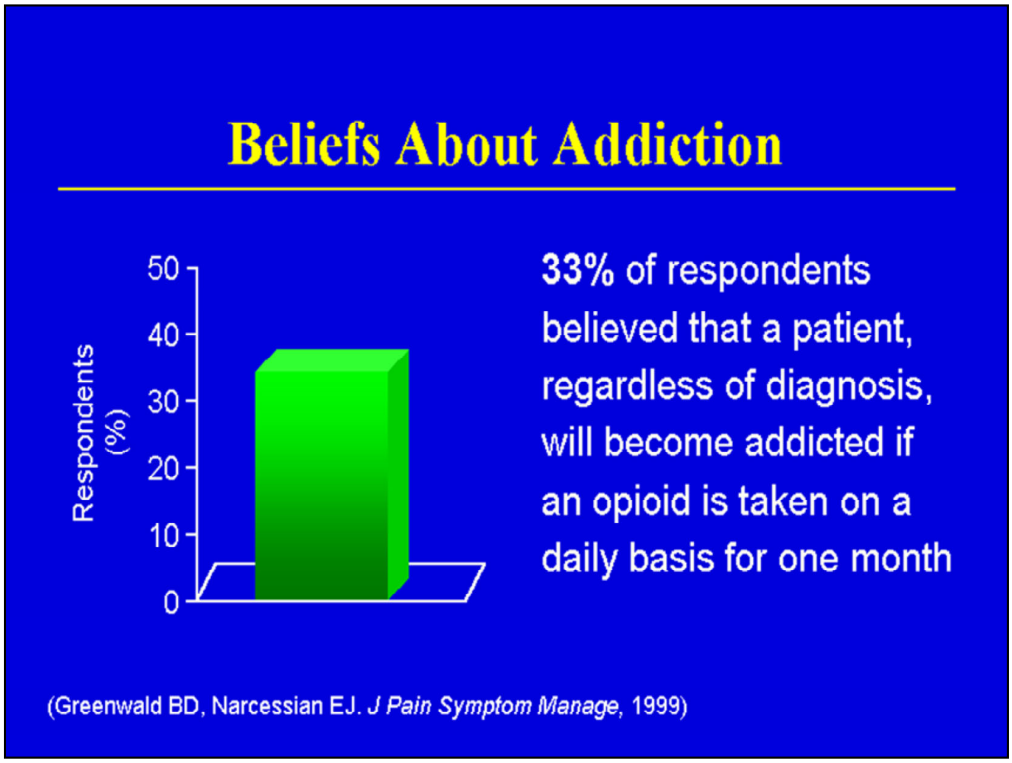

Respondents expressed the following additional concerns with prescribing practices regarding opioids[19]:

•36% believed it is illegal for a physician to prescribe methadone for pain unless certified in addiction medicine.*

•36% stated they would be resistant to fill prescriptions from a single doctor for more than one opioid.

*A physician must be certified in addiction medicine only if he or she is treating *an addict* with opioids (methadone) *for addiction.*[21]

[19]Greenwald BD, Narcessian EJ. Opioids for managing patients with chronic pain: community pharmacists' perspectives and concerns. *J Pain Symptom Manage* 1999;17:369-375.

[21]Joranson DE, Cleeland CS, Weissman DE, Gilman AM. Opioids for cancer and noncancer pain: a survey of state board members. *Fed Bulletin* 1992;79:15-49.

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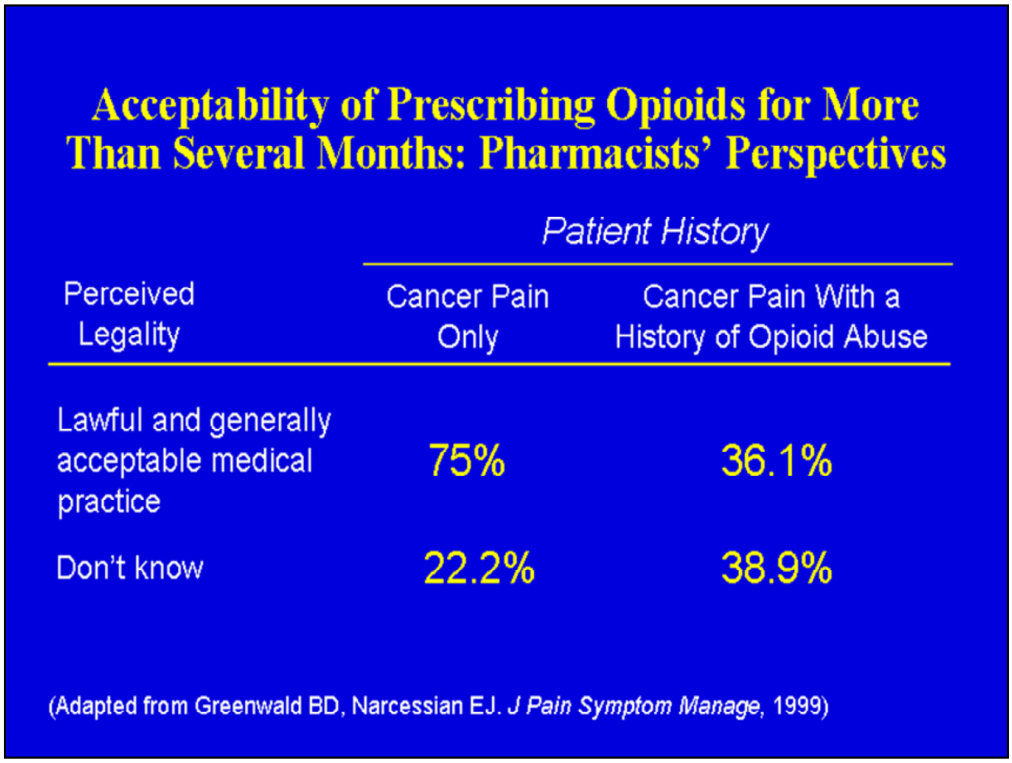

Pharmacists were surveyed regarding their opinion on the acceptability of prescribing opioids for more than several months in patients with ***cancer pain only*** and in patients with ***cancer pain and a history of opioid abuse***. The high percentage of pharmacists who responded "don't know" should be noted.

Other responses included[19]:*

Cancer pain only

•Lawful, but generally not acceptable medical practice—should be discouraged (2.8%)

•Probable violation of my standard medical practice—should be investigated (0%)

•Probable violation of federal/state controlled substance laws—should be investigated (0%)

Cancer pain with a history of opioid abuse

•Lawful, but generally not acceptable medical practice—should be discouraged (19.4%)

•Probable violation of my standard medical practice—should be investigated (13.8%)

•Probable violation of federal/state controlled substance laws—should be investigated (8.3%)

*Respondents could give more than one response.

[19]Greenwald BD, Narcessian EJ. Opioids for managing patients with chronic pain: community pharmacists' perspectives and concerns. *J Pain Symptom Manage* 1999;17:369-375.

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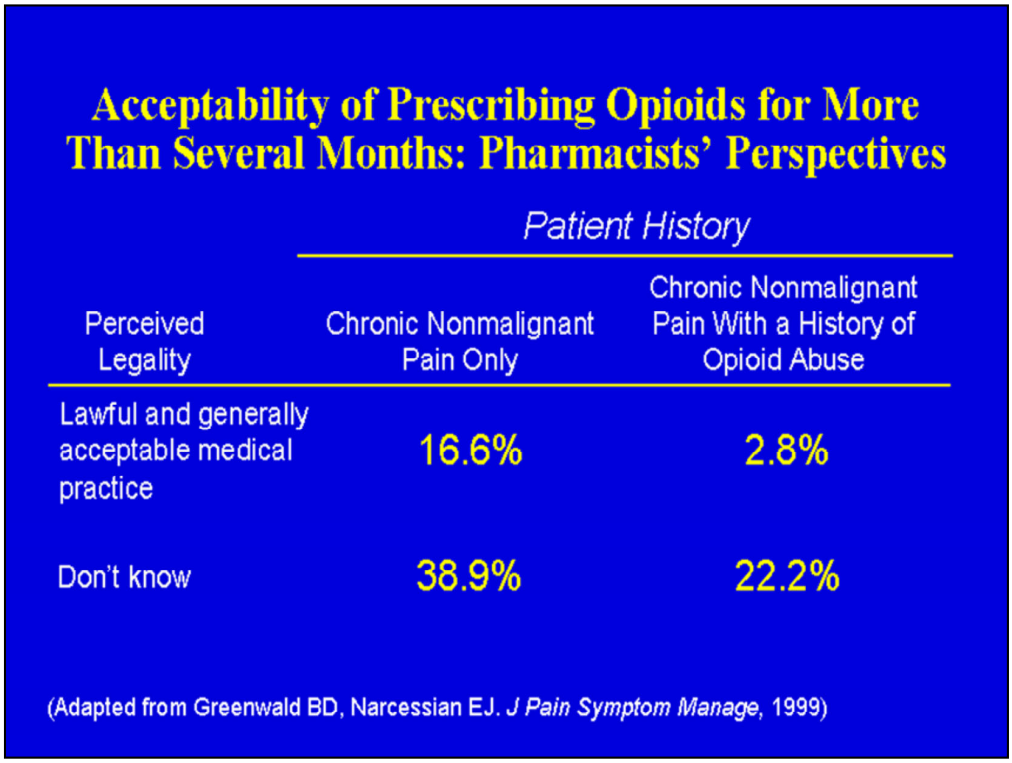

Pharmacists were surveyed regarding their opinion on the acceptability of prescribing opioids for more than several months in patients with ***chronic nonmalignant pain only*** and in patients with ***chronic nonmalignant pain and a history of opioid abuse***. The high percentage of pharmacists who responded "don't know" should be noted.

Other responses included[19]:*

Chronic nonmalignant pain only

•Lawful, but generally not acceptable medical practice—should be discouraged (47.2%)

•Probable violation of my standard medical practice—should be investigated (5.5%)

•Probable violation of federal/state controlled substance laws—should be investigated (2.8%)

Chronic nonmalignant pain with a history of opioid abuse

•Lawful, but generally not acceptable medical practice—should be discouraged (44.4%)

•Probable violation of my standard medical practice—should be investigated (36.1%)

•Probable violation of federal/state controlled substance laws—should be investigated (22.2%)

*Respondents could give more than one response.

[19]Greenwald BD, Narcessian EJ. Opioids for managing patients with chronic pain: community pharmacists' perspectives and concerns. *J Pain Symptom Manage* 1999;17:369-375.

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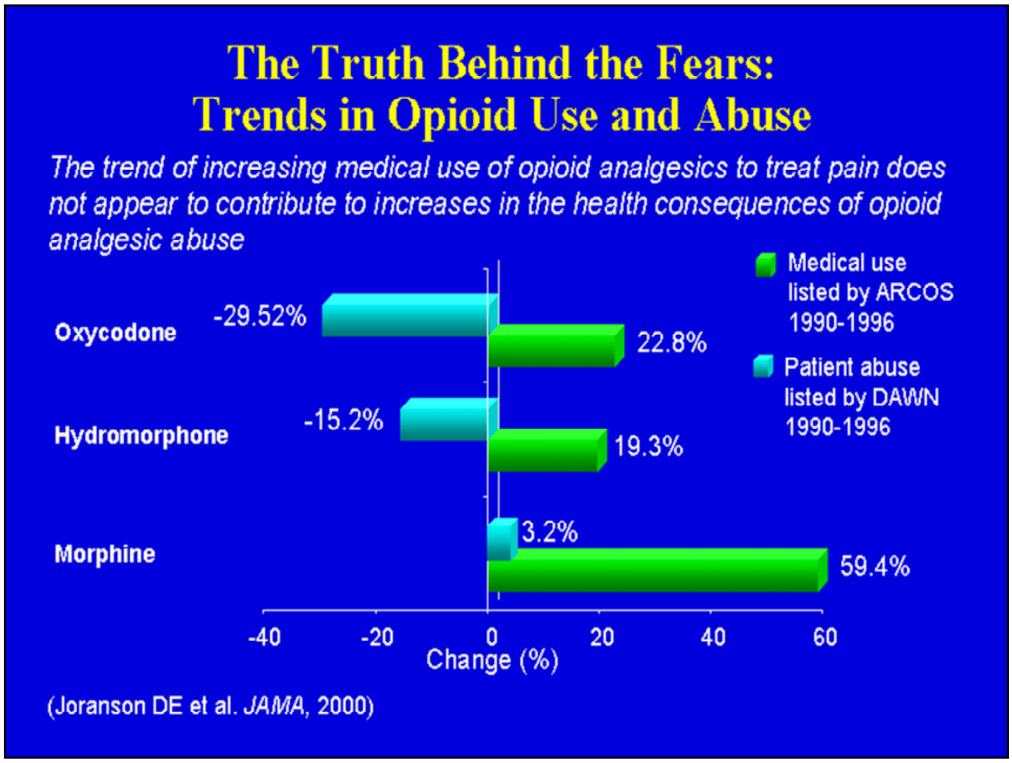
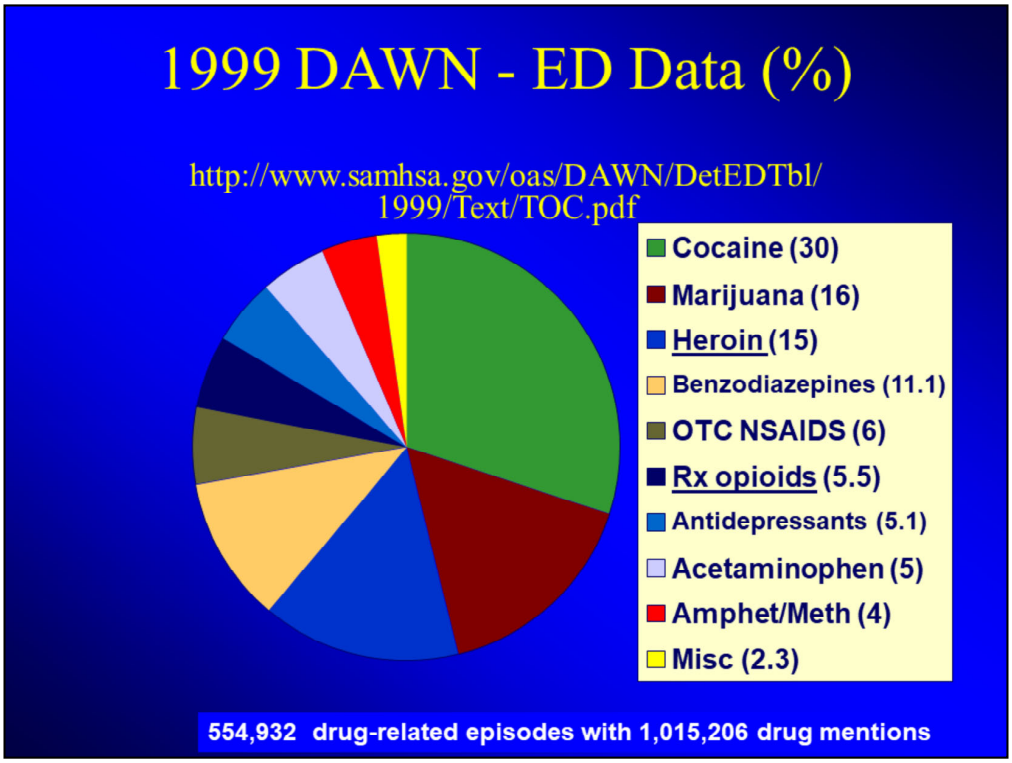


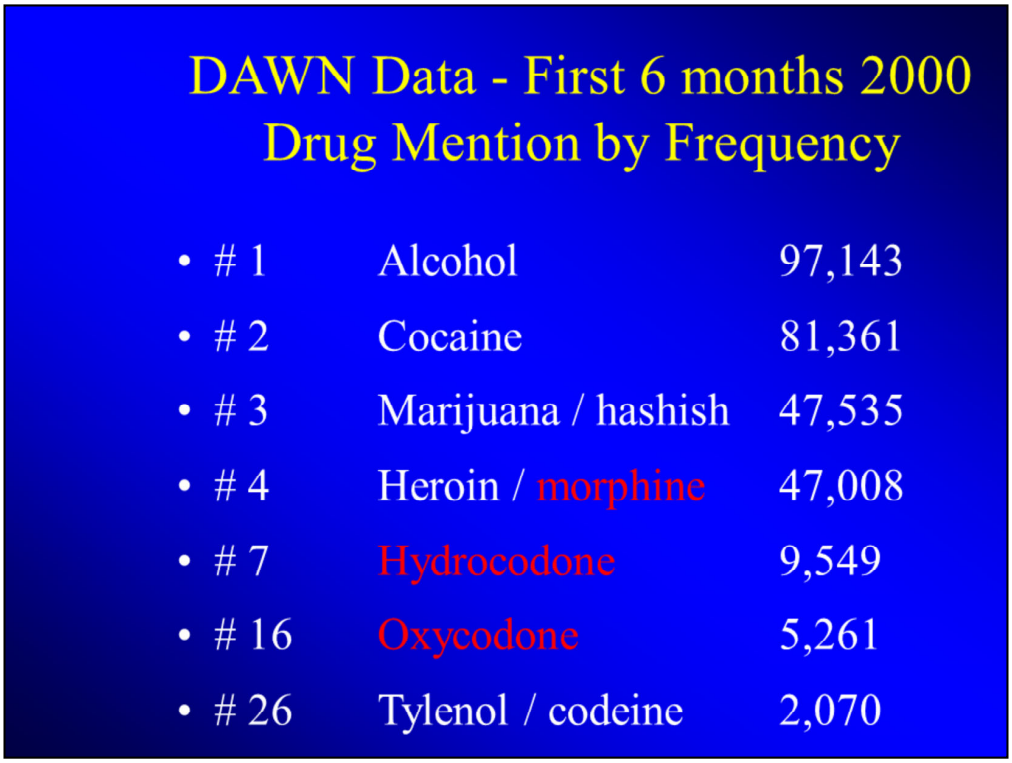
A descriptive study published in the April 5, 2000 issue of the *Journal of the American Medical Association* (*JAMA*) evaluated the trends in the medical use and abuse* of five opioid analgesics: oxycodone, hydromorphone, morphine, fentanyl, and meperidine.[26]

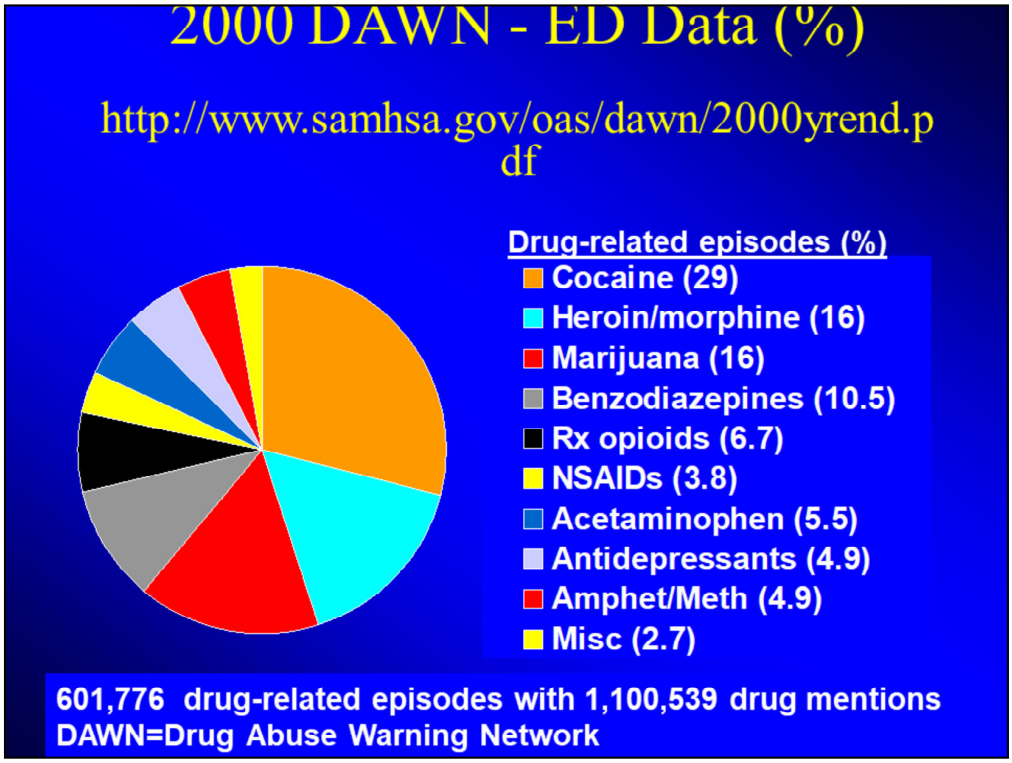
Increases in the medical use of all of the opioids were observed with the exception of meperidine.[26] During the same time period, reports of abuse (defined as the nonmedical use by patients of a substance— including prescription drugs—for psychic effect, dependence, or suicide attempt or gesture) decreased for all opioids, with the exception of morphine which increased 3%.[26]

The study concluded that "the present trend of increasing medical use of opioid analgesics to treat pain does not appear to be contributing to increases in the health consequences of opioid analgesic abuse."[26]

* Source of data
• *Abuse data:* Drug Abuse Warning Network (DAWN)
- large-scale ongoing retrospective survey of medical records used to monitor national drug abuse trends
• *Medical use data:* Automation of Reports and Consolidated Orders Systems (ARCOS)
- federal, computerized data system used to monitor the lawful distribution of controlled substances in Schedules I and II, and narcotic substances in Schedule III, from manufacturers to the retail level of


1999 DAWN - ED Data (%)
http://www.samhsa.gov/oas/DAWN/DetEDTbl/1999/Text/TOC.pdf
Cocaine (30)
Marijuana (16)
Heroin (15)
Benzodiazepines (11.1)
OTC NSAIDS (6)
Rx opioids (5.5)
Antidepressants (5.1)
Acetaminophen (5)
Amphet/Meth (4)
Misc (2.3)
554,932 drug-related episodes with 1,015,206 drug mentions


DAWN Data - First 6 months 2000
Drug Mention by Frequency
• # 1 Alcohol 97,143
• # 2 Cocaine 81,361
• # 3 Marijuana / hashish 47,535
• # 4 Heroin / morphine 47,008
• # 7 Hydrocodone 9,549
• # 16 Oxycodone 5,261
• # 26 Tylenol / codeine 2,070



The Drug Abuse Warning Network (DAWN) is maintained by the Substance Abuse and Mental Health Services Administration (SAMHSA) of the Public Health Service. DAWN is a federally-operated system that monitors more than 500 emergency departments for drug abuse trends in 21 metropolitan areas around the country.

This is the emergency department data for 2000—the most recent year for which complete data is available. Each emergency department visit is referred to as an 'episode.' There were more than six hundred thousand drug-related episodes in this sample. Up to four drugs can be mentioned as being related to the reason for each emergency department episode. More than one million drugs were mentioned. An average of 1.8 drug mentions were involved per episode.

The pie chart shows the distribution of drugs mentioned. Note that prescription opioids account for about 6.7% of all emergency department mentions. That is less than two thirds of what benzodiazepines account for, and about equal to OTC NSAIDs. Although diversion and abuse of prescription opioids is significant, they are not the only drug abuse problem.

Federal and State Controlled Substance Law

Controlled Substances Act 1970

" A prescription for a controlled substance to be effective must be issued for a legitimate medical purpose by an individual practitioner acting in the usual course of his professional practice."

"...corresponding responsibility rests with the pharmacist who fills the prescription."

21 CFR 1306.04(a)

Controlled Substances Act 1970

Allows any registrant to "administer or dispense narcotic drugs to persons with intractable pain in which no relief or cure is possible or none has been found after reasonable efforts"

21 CFR 1306.07 (c)

Drug Enforcement Administration

- What is the DEA position on prescribing controlled substances for pain experienced by:
  - someone with cancer ?
  - someone with chronic pain not due to cancer ?

Drug Enforcement Administration

"Controlled substances and, in particular, narcotic analgesics, may be used in the treatment of pain experienced by a patient with a terminal illness or a chronic disorder."

Physician's Manual: An informational outline of the Controlled Substances Act, March 1990, p 21.

Drug Enforcement Administration

"These drugs have a legitimate clinical use and the physician should not hesitate to prescribe, dispense or administer them when they are indicated for a legitimate medical purpose."

Physician's Manual: An informational outline of the Controlled Substances Act, March 1990, p 21.

Drug Enforcement Administration

"It is the position of the DEA that these controlled substances should be prescribed, dispensed or administered when there is a legitimate medical need."

Physician's Manual: An informational outline of the Controlled Substances Act, March 1990, p 21.

Summary of Federal Law

- Federal law does **not** preclude the use of opioids as analgesics for legitimate medical purposes, including treating chronic pain and treating pain in addicts.
- Federal law **does** prohibit the use of opioids to maintain an addicted state without special registration as an NTP.
- Federal law is not static (e.g., office based opioid therapy for addiction)

Slide Reference

Greenwald BD, Narcessian EJ. Opioids for managing patients with chronic pain: community pharmacists' perspectives and concerns. *J Pain Symptom Manage* 1999;17:369-375.

"The first line direct strategy for controlling most pain is reassurance, maintenance of activity, and pharmacologic analgesia."[17] The three categories of analgesic medications include[6,18]:

•Non-opioid analgesics (eg, aspirin, acetaminophen, NSAIDs)

•Opioid analgesics (eg, oxycodone, morphine, hydromorphone)

•Adjuvant analgesics (eg, tricyclic antidepressants, antihistamines, benzodiazepines, steroids, anticonvulsants)

[17]Caudill MA, Holman GH, Turk D. Effective ways to manage chronic pain. *Patient Care* 1996;30:154-172.

[6]American Pain Society. *Principles of Analgesic Use in the Treatment of Acute Pain and Cancer Pain.* 4th ed. Glenview, IL: American Pain Society; 1999.

[18]Portenoy RK. Current pharmacotherapy of chronic pain. *J Pain Symptom Manage* 2000;19:S16-S20.

Slide Reference

Portenoy RK. Current pharmacotherapy of chronic pain. *J Pain Symptom Manage* 2000;19:S16-S20.

Pharmacologic Treatment of Chronic Pain

Opioid Analgesics

- Opioids are among the most useful, versatile pharmacologic tools to treat pain
  - Morphine
  - Oxycodone
  - Hydrocodone
  - Hydromorphone
- Opioids act spinally, supraspinally, and at peripheral sites of tissue injury[23]

Guidelines for Opioid Dose Titration

- The optimal analgesic dose varies widely among patients with cancer and non-cancer pain
- Optimal management of cancer pain requires aggressive upward dose titration

(APS 1999) (Levy MH. *N Engl J Med*, 1996)

Because the AGS recognizes that older patients are at significant risk for undertreatment of their pain, they published Panel recommendations regarding this issue.

Pain in the Elderly – Nonopioid Analgesic Treatment:

- Avoid NSAIDs in abnormal renal function, bleeding diathesis, or a history of peptic ulcer[1]
- Avoid the use of more than one NSAID at a time
- Anticipate ceiling dose limitations
- GI-protective drugs do not prevent renal impairment and other interactions

Reference: 1. American Geriatrics Society Panel on Chronic Pain in Older Persons. *J Am Geriatr Soc.* 1998;46:635-651.

Pain in the Elderly – Opioid Pharmacologic Treatment: (cont'd.)

- Chronic opioid therapy, low-dose corticosteroid therapy, or other adjunctive drug therapies may have fewer life-threatening risks than long-term daily use of high-dose NSAIDs[1]

Reference: 1. American Geriatrics Society Panel on Chronic Pain in Older Persons. *J Am Geriatr Soc.* 1998;46:635-651.

Pain in the Elderly – Opioid Pharmacologic Treatment:

- Opioid analgesics can relieve moderate to severe pain, especially nociceptive pain[1]
- Fears of drug dependency and addiction do not justify the failure to relieve pain
- For occasional chronic recurrent or noncontinuous pain not controlled by NSAIDs, prescribe opioid analgesics PRN

Reference: 1. American Geriatrics Society Panel on Chronic Pain in Older Persons. *J Am Geriatr Soc.* 1998;46:635-651.

Pain in the Elderly – Around-the-Clock Dosing

For continuous pain, medications are best given on a regular around-the-clock basis[1]

- Additional doses may be required before activities known to exacerbate pain

Reference: 1. American Geriatrics Society Panel on Chronic Pain in Older Persons. *J Am Geriatr Soc.* 1998;46:635-651.

Pain in the Elderly – Opioid Pharmacologic Treatment:

- "Start low and go slow"[1]
- Elderly patients may be more sensitive to opioids, experiencing higher peak effect and longer duration of pain relief[2]
- Age-adjusted dosing recommendations are not available
- PCA should be monitored especially closely in the elderly[3]

References: 1. American Geriatrics Society Panel on Chronic Pain in Older Persons. *J Am Geriatr Soc.* 1998;46:635-651. 2. Kaiko RF. *Clin Pharmacol Ther.* 1980;28:823-826. 3. Ferrell BR, Cronin Nash C, Warfield C. *J Pain Symptom Manage.* 1992;7:149-154.

Pain in the Elderly – Around-the-Clock Dosing (cont'd.)

- Drug regimens should be as simple as possible, with the focus on decreased pain, improved function, and improved mood and sleep – not decreased drug dose[1]
- All medication management must be tailored to the individual patient

Reference: 1. American Geriatrics Society Panel on Chronic Pain in Older Persons. *J Am Geriatr Soc.* 1998;46:635-651.

Pain in the Elderly – Adjuvant Analgesic Treatment

- Adjuvant analgesic drugs may reduce pain in certain intractable pain syndromes[1]
- The use of these drugs increases the potential for adverse drug reactions, particularly in older patients[1]

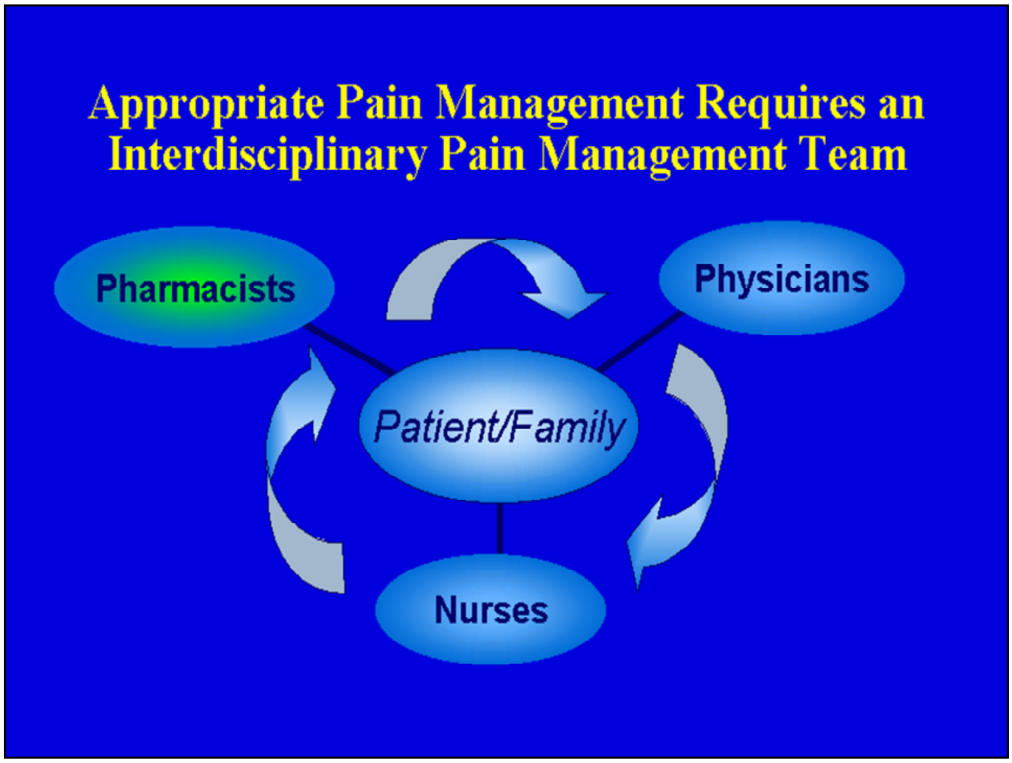
Reference: 1. American Geriatrics Society Panel on Chronic Pain in Older Persons. *J Am Geriatr Soc.* 1998;46:635-651.

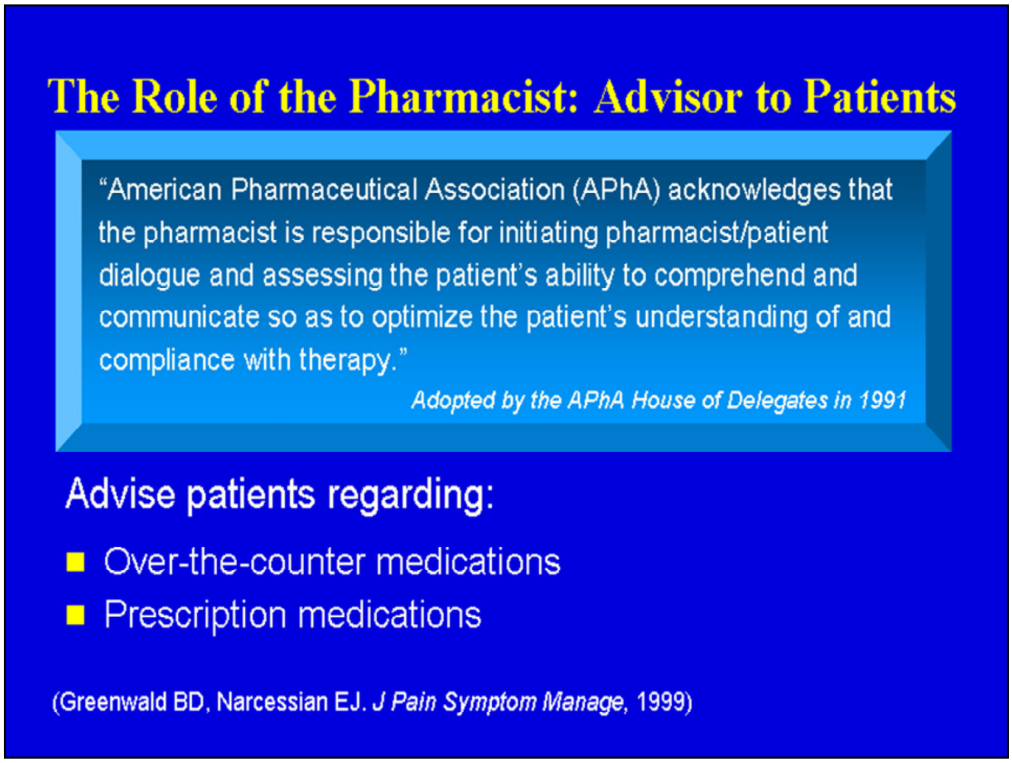
Pseudotolerance

When a stable opioid dose ceases to be effective, pseudotolerance may be a factor. The need to increase a stable dose may be due to[25]

- Increasing or new pathology
- Increased physical activity after pain diminishes
- Change in medication formulation, brand, or supplier
- Noncompliance
- Other nonpharmacologic factors

25. Pappagallo M. *J Pharm Care Pain Symptom Control*.1998;6(2):95-98.


Appropriate Pain Management Requires an Interdisciplinary Pain Management Team
Pharmacists
Physicians
Patient/Family
Nurses



As advisors to patients about medications, pharmacists take on a crucial role in impacting the outcome of a patient's pharmacotherapy.[19] A pharmacist's inadequate knowledge of issues pertinent to the pharmacological management of pain may result in adverse consequences for the patient.[19]

[19]Greenwald BD, Narcessian EJ. Opioids for managing patients with chronic pain: community pharmacists' perspectives and concerns. *J Pain Symptom Manage* 1999;17:369-375.

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Greenwald BD, Narcessian EJ. Opioids for managing patients with chronic pain: community pharmacists' perspectives and concerns.

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Discussion
and
Questions